STUDY OF ACUTE KIDNEY INJURY IN CRITICALLY ILL CHILDREN USING DIFFERENT RENAL FAILURE INDICES

A PROSPECTIVE COHORT STUDY

A DISSERTATION SUBMITTED IN PARTIAL FULFILLMENT OF THE RULES AND REGULATIONS FOR M.D. PAEDIATRICS EXAMINATION OF THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

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CERTIFICATE

This is to certify that the dissertation entitled **"Study of Acute Kidney Injury in critically ill children using different renal failure indices"** is a bonafide work of **Dr. C. Priyalatha** in partial fulfillment of the requirements for the M.D Paediatrics examination of The Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in May 2018.

DR. Indira Agarwal, MD, FISN

Professor and Head,

Department of Paediatrics,

Christian Medical College,

Vellore, Signature

Principal

DR. Anna Pulimood,

Professor

Department of Pathology

Christian Medical College,

Vellore, Signature

CERTIFICATE

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Guide:

DR. Indira Agarwal

Professor and Head,

Department of Paediatrics,

CMC, Vellore. Signature

Co-guides:

DR . KALA EBENEZER , PROFESSOR, DEPARTMENT OF PAEDIATRICS, CMC VELLORE

DR. VENKATESH , ASSISTANT PROFESSOR, PEDIATRIC NEPHROLOGY, CHILD HEALTH II,

DECLARATION

I hereby declare that the dissertation entitled **"Study of Acute Kidney Injury in critically ill children using different renal failure indices"** is a bonafide research work done by me under the supervision of Dr. INDIRA AGARWAL, Professor & Head of Paediatrics, Christian Medical College, Vellore, in partial fulfillment of the requirements for the M.D Paediatric examination of The Tamil Nadu Dr. M.G.R Medical University, Chennai to be held in May 2018.

Name : Dr. C. Priyalatha
Post Graduate Registrar
Paediatrics
Christian Medical College
Vellore

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DR. Indira Agarwal , MD,FISN

Professor and Head,

Department of Paediatrics,

Christian Medical College,

Vellore,

Signature

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CONTENTS

INTRODUCTION

1. INTRODUCTION

Acute Kidney Injury (AKI), previously known as Acute Renal failure, is an abrupt decline in renal excretory function characterized by a reversible increase in the serum creatinine and nitrogenous waste products. The underlying pathophysiology includes decreased renal perfusion due to various causes resulting in decreased urine output, rising serum creatinine, deranged fluid and electrolyte homeostasis, reduction in the immunity thereby affecting various organ systems.(1)

Acute Kidney Injury is the manifestation of many disorders that affect the kidney and is common in hospitalized patients, especially in critically ill patients. It is diagnosed mostly along with other illnesses especially in critically ill children.(1)

AKI can be divided into pre-renal injury, intrinsic kidney disease (including vascular insults) and obstructive uropathies. The prognosis of AKI is highly dependent on the underlying cause of the injury. Children are found to be more susceptible to injury than adults and more so in female children. Children who have AKI as a component of multisystem failure have a much higher mortality rate than children with intrinsic renal disease.(1)

The incidence of AKI is highly varied and its pattern in different countries is affected by various factors namely definitions, ethnic groups, etiology and economic conditions. Acute Kidney Injury has been reported to be on rise in both developing and developed countries and it is independently associated with increased mortality and morbidity in children and adults with subsequent development of renal dysfunction (chronic Kidney Disease) (1,2).

The incidence of AKI based on definitions varies from more than 5000 cases per million per year for non-dialysis requiring AKI to 295 cases per million people per year for dialysis – requiring condition. The incidence of AKI was four fold higher in critically ill patients (36.1%) compared to non critically ill patient (09%)(3). The incidence of AKI in southern India is found to be 5% in hospitalized patients and 30 % in PICU. In a prospective study done in southern India it was found that the incidence of AKI was 25.1% in critically ill children with 27.8% in patients requiring RRT.(3)

It has been found that about two million people die due to AKI annually and the mortality increases when there is decline in the renal function, after the admissions in to the intensive care unit. This entity refers to the continuum of kidney insult that starts long before sufficient loss of excretory kidney function can be sensed. Hence this condition is a significant diagnostic and therapeutic challenge for clinicians. Moreover, there is no specific treatment developed so far that can reduce acute kidney injury or speed up the recovery.

There is a need to decrease the growing burden of Acute Kidney Injury and its complications globally. The presence of AKI is associated with longer PICU and hospital stay, with higher mortality imposing the significant burden to healthcare system. AKI should no longer be a death sentence for these people. Nobody should die of preventable and treatable AKI by 2025 (as per the 0by25 initiative).(4) Adequate measures should be taken in the prevention with early detection and management, and follow-up. These efforts will decrease mortality and the long term burden of AKI leading to chronic kidney Disease (CKD).

As AKI presents with varied clinical manifestations, there have been several definitions in the past to classify or define AKI, however no single comprehensive definition is available so far. The different renal indices like pRIFLE, AKIN and KDIGO were used to compare, the outcomes, making it a simple method to diagnose AKI and predict its outcome.

As multiple definitions have been used for AKI, the lack of uniformity has lead to a significant difference in the incidence of AKI reported so far thus affecting the overall and renal outcome. AKI now being one of the major public health problems associated with long term complications particularly due to development of CKD and increased financial burden. Hence with such high incidence of AKI in critically ill patients there is a need for early detection of AKI before a significant rise in serum creatinine level and renal damage occurs. Appropriate diagnostic evaluation is necessary to recognize AKI, so that specific treatment and interventions are available in order to reverse the renal injury thereby preventing further progression.

There is a significant difference in incidence and staging of AKI using pRIFLE, AKIN, and KDIGO. All three definitions correlate highly with outcomes and show very good inter-stage differentiation. pRIFLE is sensitive, identifying a greater number of mild AKI cases. AKIN is advantageous as it does not require height or baseline creatinine values. KDIGO offers applicability to both pediatric and adult populations and has a diagnostic time frame (7Days or more) that is less restrictive than AKIN.(5)

Multiple definitions for AKI have obviously led to a great disparity in the reported incidence of AKI making it difficult or even impossible to compare the various

published studies focusing on AKI.(6–9). Therefore, it became crucial to establish a consensual and accurate definition of AKI that could ideally be used.

The present study aims to compare the three different criteria for diagnosing AKI and their ability to detect AKI early, predict morbidity and mortality and thus improve outcome in our hospital setting. We hope to be able to establish the appropriate criteria for practical use in our PICU setting.

AIMS AND OBJECTIVES

AIMS:

To study the correlation among the different renal failure indices in predicting the outcome of AKI in critically ill children.

PRIMARY OBJECTIVE:

To compare the ability of different Renal Failure Indices to diagnose Acute Kidney injury (AKI) and predict its outcome in critically ill children

SECONDARY OBJECTIVE

1. To study the incidence of AKI in children admitted in PICU.

2. To study the clinical course of AKI, the length of stay, mortality and the risk factors associated with poor outcome.

REVIEW
OF
LITERATURE

REVIEW OF LITERATURE

Acute Kidney Injury is a condition characterized by abrupt onset of impairment in the renal function resulting in the imbalance of fluid and electrolyte homeostasis (10). Acute kidney Injury due to Ischemic and hypoxic causes, take place in the kidneys much earlier than the rise in serum creatinine. It is a serious and significant clinical problem especially in children, with critical illness resulting from different clinical conditions. Since renal hypoperfusion may co exist with any stage of AKI, the difference between pre renal and renal causes is difficult and this helps us to diagnose AKI using oliguria criteria, in the presence of normal serum creatinine level (5). In a study involving 2,644,263 children, 10,322 children developed AKI (3.9/1000 admissions). 19% of the AKI cohort was ≤1 month old, the highest incidence was seen in children 15–18 years old (6.6/1000 admissions).(11)

AKI in children can occur at any point, either at the time of admission or during the stay in hospital. The etiology of AKI differs in our country from western setup due to the prevalence of different diseases. There are only few studies available in the literature from our country when compared to the west. Much information is still needed to study the diseases or conditions causing AKI aiming to identify it at the earliest.(4) AKI is more common in critically ill children compared to non-critically ill children.(12)

Keenswijk et al in their single center retrospective cohort study of 28,295 children, found 167 cases of AKI (5.9cases/1000children). The median age of children with AKI was 6.1 years, with 50.8% of children affected being males. The mortality was

15% and 16% progressed to CKD (13). The incidence of AKI was found to be 25.1% in PICU and 5.25% in the wards.

Etiopathogenesis:

Acute Kidney Injury is the manifestation of many disorders that affect the kidney and is common in hospitalized patients, especially in critically ill patients. It is diagnosed mostly along with other illnesses especially in critically ill children.

Raes A et al reported that the diarrhoea associated with HUS during summer months was the most common cause (13) The etiologies found were infections 55.4%, AGN were 16.9%, cardiac disease 4.85%, envenomations 4.2%, HUS 3.6%. (3) young age (HR 0.89; 95% CI 0.83, 0.95), shock (HR 2.65; 95% CI 1.32, 5.31), sepsis (HR 3.64; 95% CI 2.20, 6.01 and need for mechanical ventilation were independent risk factors for AKI.(12) Sepsis-associated AKI has a higher incidence rate in critically ill children. (14) Renal vein thrombosis and cortical necrosis are the important causes of AKI in neonates, Hemolytic Uremic Syndrome is common in young children, and Rapidly Progressive Glomerulonephritis (RPGN) generally seen in older children and adolescents.

Nephrotoxic drugs are another important cause of AKI in children and are reported to be agents are responsible for 16% of AKI. NSAIDS, antibiotics, amphotericin B, antiviral drugs, ACE and calcineurin inhibitors, radio-contrast agents and cytotoxic drugs which are some of the agents which cause AKI in children(15). Milrinone is an inotropic drug used in a variety of clinical settings in children may also worsen the renal function in children with pre existing AKI (16).

Exposure to teratogenic drugs like angiotensin receptor blockers, angiotensin-converting enzyme inhibitors and nonsteroidal anti-inflammatory drugs during pregnancy

may lead to AKI in newborns interfering with nephrogenesis. Significant greater risk of developing AKI for patients treated with morphine, paracetamol and also with glucocorticoids, betalactam antibiotics, opioids, and non-steroidal anti-inflammatory drugs. (17)

A study was conducted in our insitution by Agarwal I et al to assess the clinical profile of children admitted with acute renal failure and to identify factors associated with poor outcome in 1998. Fifty-four children (age one month to 12 years) with acute renal failure were studied over a period of five years. The leading precipitating causes for renal failure were acute gastro-enteritis (85%), underlying renal pathology (43%), proven sepsis (22%) and suspected sepsis (22%). The main presenting complaints were diarrhoea (86%),oliguria (72%), rapid respiration (37%), oedema (37%), vomiting (19%) and seizures (13%).(18) Interventions included were Mechanical ventilation and dialysis. The mortality was 52% and predominantly occurred in patients with sepsis (83%)

In a study by Marco Zaffenello et al in their studies on early diagnosis of acute kidney injury with urinary biomarkers have shown that very low birth weight, prematurity, patent ductus arteriosus, Nonsteroidal anti-inflammatory drugs and maternal receipt of antibiotics were associated with the development of AKI in neonates (19).

In a prospective study by Krishnamurthy et al, in southern India conducted on 2376 children over a period of nine months, to study the clinico-etiological profile found that there are different causes of AKI. Infections,(55.4%), with pneumonia (15%) and sepsis (7.8%),glomerulonephritis,(16.9%) cardiac disease (4.8%) envenomations(4.2%) and HUS (3.6%) were predominant causes in developing countries . (3)

A study by Amira-Peco-Antic described that AKI results from renal ischemia, nephrotoxins and sepsis, rather than diffuse renal disease, like glomerulonephritis, interstitial nephritis, renovascular disorder and thrombotic microangiopathy.(19)

Sodeghi Bojd S et al in their study on 303 children over a period of 20 months from April 2012- December 2014 in PICU, found that the most common PICU admission diagnoses in AKI were neurologic 85 (28.05%), followed by heart diseases 52 (17.18%) and 31 (10.23%) for respiratory diseases. AKI was more prevalent in renal (43.5%) and endocrine (5.4%)patients .(20)

Acute tubular necrosis, Acute interstitial necrosis and constriction of intrarenal vessels and tubular obstruction are the known mechanisms of injury.(15) Impaired renal perfusion and direct renal tubular injury are the two different mechanisms causing AKI. The oxygen gradient from cortex to glomeruli makes the renal tubules vulnerable to risk of hypoxic and oxidative injury. Sepsis is the most important cause of AKI in children, which is secondary to inflammatory mediator effects on renal vascular endothelium and alterations in the microvascular perfusion of the glomerulus. Another leading cause of AKI in children is cardiopulmonary bypass. Several “combination syndromes”, e.g. hepato-renal, pulmonary-renal, and cardio renal syndromes associates AKI to other visceral injury.(21)

Risk Factors:

The risk factors contributing to hospital AKI are mechanical ventilation, stem cell transplantation, use of vasoactive drugs and diuretic-resistant hypervolemia.(19)
A study by Sutherland SM et al reported that Shock, septicemia, intubation/mechanical ventilation, circulatory disease, cardiac congenital anomalies , and extracorporeal support were associated with AKI.(22) A study of the Global scenario suggests that the impact of sepsis on AKI is significant and contributes to all aspects of ICU-related morbidity-which includes long duration of stay, ventilation, secondary infections, and mortality, in addition to long-term survivor's issues.(14)

Potentially modifiable risk factors for the development of AKI such as nephrotoxic medication exposures are of paramount importance. Hanna et al in their study stated that the neonatal kidney is predisposed to nephrotoxic AKI and methods should be developed to minimize and prevent nephrotoxic AKI in neonates through a multi-disciplinary approach aiming at earlier recognition and close monitoring prevent nephrotoxic AKI in neonates through a multi-disciplinary approach aiming at earlier recognition and close monitoring of nephrotoxin induced AKI. Preterm babies are born with incomplete nephrogenesis and are at risk for chronic kidney disease. The use of nephrotoxic medications in the NICU should be avoided.(23–25).

Diagnostic criteria:

Acute kidney injury has more than 35 different definitions in the past few decades.(26). Many of those definitions are complex. However the more commonly used were based on the urine output (UO) and / or serum creatinine (S Cr) criteria. An increase

in basal serum creatinine of at least 44.2 mmol / L (0.5mg/dl), a decrease in creatinine clearance of at least 50% or the need for renal replacement therapy were the most frequent definitions used for AKI in clinical practice.(8) Where UO has been used to define AKI, it is generally considered that a value less than 400-500ml/day could be an indicator. In their study Prowle JR et al stated that oliguria is strongly associated with the development of new AKI-Cr; but, majority of oliguria are not associated with rise in serum creatinine. Oliguria alone is at best only a fair predictor of AKI-Cr. However, in the presence of hemodynamic compromise or increasing vasopressor dose, it serves as a useful screening tool to trigger other early biomarkers of renal injury with the goal of achieving a more accurate and timely identification of patients at risk of AKI.(27)

In 2002, Acute Dialysis Quality Initiative (ADQI), group for the study of AKI, came with the purpose of defining AKI. They considered that the ideal AKI definition would have to accomplish the following criteria; easy clinical applicability, sensitivity and specificity, consider baseline serum creatinine variation and also acute on chronic phenomenon. This definition classified AKI according to severity (mild v/s Severe) and its timing of occurrence (early v/s late). By fulfilling these criteria this classification should allow the recognition of children whose kidney function was slightly affected (high sensitivity but low specificity) as well as patients with severe kidney function deterioration (high specificity with diminishing sensitivity). (28)

Different renal indices like pRIFLE, AKIN and KDIGO were developed over the last decade to compare, the outcomes, making it as simple method to diagnose AKI and predict its outcome.

p-RIFLE Criterion:

In 2004 the ADQI proposed the RIFLE classification for AKI; the Risk, Injury, Failure, Loss of Kidney function and End stage kidney disease, the first evidence based consensus. This classification included three grades of severity of AKI (Risk, Injury and Failure and two outcome (loss of kidney function and end stage renal disease) according to the relative changes in the serum creatinine and urine output. The criteria that led to the higher stage should be considered. This criterion has shown a good relevance for diagnosing and classifying the severity of AKI and for monitoring the progression as well as comparable predictive ability for mortality. This definition was modified and evaluated in critically ill paediatric patients and termed p-RIFLE criteria. It was based on the estimated creatinine clearance and urine output.

Table 2.1: pRIFLE classification of AKI

	Estimated CrCl	**Urine Output**
Risk	eCrCl decrease by 25%	< 0.5 ml/kg/h for 8 h
Injury	eCrCl decrease by 50%	< 0.5 ml/kg/h for 16 h
Failure	eCrCl decrease by 75% or eCrCl < 35 ml/min/1.73m^2	< 0.3 ml/kg/h for 24 h or anuric for 12 h
Loss	Persistent failure > 4 weeks	
End Stage	End – stage renal disease (persistent failure > 3 months	

eCrCl, estimated creatinine clearance.

Taken from: International Journal of Contemporary Pediatrics*Srinivasa S et al. Int J Contemp Pediatr. 2016 May;3(2):398-402*

pRIFLE criteria provides a uniform definition for AKI making it a simple tool in clinical research, very useful for early recognition and classification of AKI and to correlate with clinical outcome.(5)

AKIN Criterion:

In 2007, the Acute Kidney Injury Network (AKIN) group proposed a modified version of the RIFLE classification aimed to improve the sensitivity of AKI criteria. According to this criterion the diagnosis of AKI is to be considered only after achieving an adequate status of hydration and after excluding urinary obstruction. The AKIN criteria rely on S Cr and not on GFR changes and baseline S Cr is not necessary. It requires at least 2 values of S Cr obtained within a period of 48 hours.

AKI is defined by the sudden decrease (in 48 hrs) of renal function defined by an increase in absolute S Cr of at least 26.5 micromol/ L (0.3mg/dl) or by a percentage increase in S Cr >50% (1.5 times of the baseline) or decrease in the urine output with documented oliguria less than 0.5 ml/kg/hr for more than 6 hours. The stage I corresponds to the Risk and stage 2 correspond to the Injury and Failure classes respectively. The stage 3 also considers the patients requiring renal replacement therapy independent of the stage they are in at the point of RRT. The two outcome classes namely, the loss of kidney function and End Stage Renal Disease (ESRD) were removed from this classification. These modifications are based on the cumulative evidence that even small increase in S Cr are associated with a poor outcome.(1).

The following recommendation was made:

Table 2.2: AKIN classification of AKI

Stages	Serum Creatinine Criteria	Urine Output
Stage 1	Increase in serum Creatinine ≥ 0.3 mg/dl (≥ 26.4μmol/l) or increase to ≥ 150% to 200 % (1.5 fold to 2 fold from baseline	< 0.5 ml/kg/h for 6 h
Stage 2	Increase to >200% to 300 % (> 2 fold to 3 fold) from baseline	< 0.5 ml/kg/h for >12 h
Stage 3	Increase in serum creatinine to >300% (>3 fold) from baseline or serum creatinine ≥ 4.0 mg/dl (≥354μmol/l) with acute increase of atleast 0.5mg/dl	<0.3 ml/kg/h for 24 h or anuria for 12 h

International Journal of Contemporary Pediatrics, *Srinivasa S et al. Int J Contemp Pediatr. 2016 May;3(2):398-402*

KDIGO criterion:

In 2012, a modified definition that merged RIFLE, p RIFLE and AKIN criteria has been proposed Kidney Disease Improving Global Outcome (KIDGO). This aimed to establish uniform definition and classification of AKI expected to be adopted for research and publication. According to this criterion,(29) AKI was defined by any of the following

Modifications also allowed for a child with estimated GFR (eGFR) <35 ml/min per 1.73m2 to be included in stage 3, in contrast with the adult criterion of ≥ 4 mg/dl serum creatinine, which would be unusual in infants and young children. Extension of the

diagnostic timeframe for a serum creatinine rise to seven days allows the inclusion of patients with late onset AKI.

Table 2.3: KDIGO classification of AKI

Stage	Serum Creatinine Criteria	Urine Output
Stage 1	Increase by 1.5 - 1.9 times baseline within 7 days or increase to ≥ 0.3 mg/dl (26.5 μmol/L) within 48 hours	< 0.5 ml/kg/h for 6 to 12 hours
Stage 2	Increase by 2 – 2.9 times baseline	< 0.5 ml/kg/h for ≥12 h
Stage 3	Increase by ≥ 3 times baseline or increase to ≥ 4 mg/dl (353 μmol/l) or renal replacement therapy initiation or in patients younger than 18 years, decrease in eGFR to < 35ml/min/1.73m^2	<0.3 ml/kg/h for ≥24 h or anuria for ≥ 12 h

The KDIGO AKI criteria have been validated in hospitalized children with both critical and non-critical illness. It is recommended that the KDIGO AKI definition and staging be used to guide clinical care, and as a standardized inclusion and outcome measure in AKI paediatric studies.

A standardized definition of AKI was proposed by the Kidney Disease: Improving Global Outcomes (KDIGO) AKI working group in 2012 and is validated in

pediatric populations subsequently. This definition identifies and stages AKI based on changes in serum creatinine from baseline or urine output as detailed in the table below.

Baseline creatinine is defined as the lowest serum creatinine value in the previous 3 months, estimating the baseline glomerular filtration rate (GFR) using the original Schwartz equation. Where no previous serum creatinine measures are available, it is recommended to use a presumed baseline of 120 mL/min/1.73 m^2. In the future, we may see these definitions further expanded to include criteria using serum Cystatin C or urinary biomarkers such as Neutrophil Gelatinase Associated Lipocalin (NGAL), both of which have recently been shown to represent earlier markers of AKI and recovery than serum creatinine.(30)

Basu RK et al described in his study applied two biochemical parameters namely serum creatinine and urine output measurements, cumulative fluid overload (%), serum creatinine corrected for fluid balance, and KDIGO AKI stage as a marker for diagnosing and staging AKI. (31)

Comparison of AKI Definitions

The incidence, causes and diagnosis of AKI in critically ill children varies based on the population studied, definitions used and the level of care given. (32)

Various studies have shown that use of the definitions of AKI (RIFLE and AKIN) has increased to a greater extent in the literature, indicating the acceptance of the above definitions. However, diagnosis of AKI based on any of the above classification, has poor clinical outcome. Higher the RIFLE class greater the mortality with a longer stay in

Intensive care unit (ICU).(33) The RIFLE/AKIN classifications are essential for understanding the epidemiology, etiology, appropriate management, and prognosis of AKI and has shown promising results as good prognostic tools for the assessment of morbidity and mortality in AKI.(34)

AKI is commonly seen in critically ill children, especially in younger age and in females with septicemia and MODS. It has been shown that pRIFLE is a better diagnostic criteria in early detection of AKI and reduction of their morbidity and mortality.(4). Paediatric RIFLE criteria may guide in the early identification of patients at risk for AKI and in the initiation of therapy.(35)

In a study by Srinivasa S et al, on critically ill children from December 2013 – May 2015 found higher incidence of AKI was diagnosed by AKIN criteria in comparison to pRIFLE criteria. AKI occurred in 178 (26.1%) PICU patients through pRIFLE, risk in 108(15.9%), injury in 51 (7.5%) and failure in 19 (2.8%), while by AKIN criteria, AKI occurred in 248 (36.5%) patients, with 93 (37.5%) in Stage 1, 88(35.5%) in Stage 2 and 67(27 %) in Stage 3. For pRIFLE criteria odds ratio (OR) for mortality was 0.92, 5.22 and 73.71 for Risk, Injury and Failure stage respectively. Results for AKIN criteria were, OR of 2.98, 3.60 and 3.15 for stage 1, 2 and 3 respectively for mortality rate. Both criteria had good association with mortality.(28)

Critical and noncritical AKI is highly prevalent with a rising incidence and is associated with high mortality, particularly in the ICU setting. The RIFLE/AKIN classifications have been shown to be good prognostic tools for morbidity and mortality associated with AKI(34) .

Kavaz Asli et al, in a prospective study done at PICU from June 2009 – December 2010 stated that although both pRIFLE and AKIN criteria were very helpful in the detection of patients with AKI even in the early stages of it, pRIFLE seems to be more sensitive in paediatric patients(36)

Acute kidney injury is a clinical syndrome defined by a rise in serum creatinine and/or fall in urine output as per KDIGO classification(37).The KDIGO definition and staging criteria were found to be more appropriate for defining the epidemiology of AKI with insufficient evidence to support their widespread application to clinical care (38)

Table:2.4 Comparison on the incidence of AKI based on KDIGO, AKIN and pRIFLE criteria based on various studies

S.No	Study	Year/Population	pRIFLE	AKIN	KDIGO
1	Sutherland et al USA	2006-2010 N=14795	17.03	12.43	13.43
2	Jiang Li et al China	2012 N=3107	15.6	13.13	16.97
3	Kavaz et al	2012 N=189	35.9	33.3	-
4	Zeng et al	2014 N=31970	16.1	16.6	18.3
5	Luo et al	2017 N=438	46.9	38.4	51

There were only 4 reports in literature of studies which compared all the 3 AKI definitions for diagnosis of AKI. Most other studies compared any two of these criteria. The first was a report by Xuying Luo etal in a prospective study on 438 adult patients. AKI was diagnosed using the three different criteria based on Serum Creatinine or Urine output or both However in the final analysis, diagnosis was made only using the Serun creatinine criteria(39). The only other study in literature was by Sutherland et al, also a retrospective study and the only one to be done in children, from Standord Univerity and Cincinnati Childrens Hospital, USA used again the serum creatinine criteria. The detailed results of both studies are depicted below. The study was able to show that pRIFLE, AKIN and KDIGO exhibited a good interstage discrimination(40)

Therefore, all these definitions have their own limitation. For wide acceptance, a new classification was needed to establish an early diagnosis of AKI that would be a simple and useful clinical tool.(11).

Outcome:

Children with failure at presentation required RRT compared to other stages. (13) In their study Shah et al stated that Children with AKI coexisting MODS have a increased risk of mortality compared to children with intrinsic renal disease alone. Recovery from intrinsic renal disease is also highly dependent on the underlying etiology of the AKI.(41)

A study on 4000 critically ill children by Basu et al., there was increase in the mortality and the length of the hospital stay by four fold in children with AKI, especially if associated with multi-organ failure, hematopoietic stem cell or post transplant, extra-

corporeal membrane oxygenation (ECMO), or ARDS. AKI affects between 2.7 and 28% of children following CPB and carries a notable increased morbidity risk, including longer duration of mechanical ventilation and hospital length of stay. For these children, even a small creatinine rise of ≥25% is a significant risk factor for AKI. Collectively, these studies strongly suggest that AKI represents a serious burden to the pediatric patient population .(21) Mechanical ventilation and RRT initiation were associated with higher likelihood of death (ARR = 13.23, 95% CI: 1.90 - 92.04, and ARR = 2.20, 95% CI: 1.18 - 4.12, respectively)(42) Children with AKI had a longer duration of hospital stay and higher mortality.

In a retrospective cohort study by Cabral FC et aldone over 1 year periodin 375 patients found that the Paediatric index of mortality 2 score predicted a mortality rate of 9% among non acute kidney injury patients versus a mortality rate of 16% among acute kidney injury patients (p=0.0060). Patients classified as having severe acute kidney injury(paediatric-modified Risk. Injury, Failure, Loss,End –Stage renal disease I+F) exhibited higher mortality (14.1%,p+0.001) and prolonged PICU length of Stay (median,7d,p=0.001). In a retrospective study by Alkandari et al found that the Pediatric Index of Mortality 2 tends to underestimate mortality in pediatric patients with severe acute kidney injury.(43) AKI was associated with increased mortality (adjusted odds ratio (OR) = 3.7, 95% confidence interval (95% CI) = 2.1 to 6.4, using the standard bSCr method; OR = 4.5, 95% CI = 2.6 to 7.9, using normative b SCr values in all patients). AKI was independently associated with longer PICU stay and required mechanical ventilation. (44)

The mean duration of PICU stay was longer, requirement of mechanical ventilation and mortality rates were higher in patients with AKI when compared to patients without AKI.(36,45,46). In a study done in Southern India by Krishnamurthy et al., a total of 23 (79.3% of survivors) children with AKI had complete renal recovery while 6 (20.7% of survivors) had partial renal recovery at discharge. In AKI stage 1, out of the survivors, 11 (91.7%) had complete renal recovery while 1 (8.3%) had partial renal recovery at discharge. In AKI stage 2, 4 (66.7%) had complete renal recovery while 2 (33.3%) had partial renal recovery at discharge. In AKI stage 3, 8 (72.7%) had complete renal recovery, while 3 (27.3%) had partial renal recovery at discharge (differences not significant).(47)

A total of 15 patients (27.8%) required dialysis. Nine (60%) underwent peritoneal dialysis while 6 (40%) underwent hemodialysis. The mortality among children requiring RRT was similar to children not requiring RRT (46.7% vs. 46.2%). Requirement of RRT was not related to age or the etiology of AKI They concluded that.AKI is independently associated with poor outcomes in critically ill children. Serum creatinine, which is considered the main biomarker of AKI is actually a late marker of injury and can cause a delay in diagnosis.(48)

In an un published retrospective study done at PICU in 2008 by Jacinth et al. at Christian Medical College Vellore on The profile of AKI in children with shock and the utility of cystatin C as early biomarker in AKI , found that out of 93 children, the overall mortality due to shock among children with AKI was 53%.. Cystatin-C as a biomarker had sensitivity of about 59% and 79% specificity.

Management:

Volpon LC, et al stated that Inotropic score greater than 10 was a risk factor for acute kidney injury severity. About 35% of patients with acute kidney injury who survived were discharged from the PICU with an estimated creatinine clearance less than 75 mL/min/1.73 m2 and one persisted with altered renal function 6 months after PICU discharge. Age 12 months old or younger was a risk factor for estimated creatinine clearance less than 75 mL/min/1.73 m2 at PICU discharge. (46)

It was also noted that any small change in renal function has greater clinical effect resulting in poor outcome. There has been change in the term from Acute Renal Failure to AKI, in order to have a standard definition there by to include the clinical spectrum from mild rise in serum creatinine level to the development of kidney disease and also to emphasis on the reversible nature of Acute kidney insult, with the need to promote organ protection and prevent further injury. Once earlier identification of renal injury is achieved both supportive and renal replacement therapy can be instituted and further insults can be prevented.

KDIGO guidelines stated that the assessment of cardiac function and intra-abdominal pressure should be considered while diagnosing AKI. Laboratory parameters – including S Cr, blood urea nitrogen, and electrolytes, complete blood count and differential should also be made. Urine analysis and microscopic examination as well as other urinary biomarkers may be helpful in determining the underlying cause of AKI. Imaging tests, especially ultrasound, should be performed in the evaluation for patients with AKI. (49)

Oliguria (61.5%, $p < 0.0001$) and hypervolemic signs (38.5%, $p = 0.03$) were more common among patients with RIFLE class failure. They also had the highest mortality (53.9%, $p = 0.01$). Oliguric patients were ~ 23 times more likely than their non-oliguric counterparts to be initiated on renal replacement therapy (RRT) (RR = 23.38, 95% CI: 3.07 - 178.16). Diuretic infusion was also a strong predictor for RRT initiation (RR = 10.00, 95% CI: 2.77 - 36.12). Hypervolemic patients were twice more likely to die during hospitalization in both unadjusted and adjusted models (RR = 2.06, 95% CI: 1.09 - 3.90, and a RR = 2.45, 95% CI: 1.09 - 5.51, respectively). (42)

In recent times the new biomarkers have been used in the diagnosis of AKI. However these biomarkers have been validated against a gold standard which is a consensus definition based on S Cr measurements. This definition should evolve on the basis of evidence. (50)

A study done by Vasudevan et al on the use of peritoneal dialysis for AKI stated that renal replacement therapy (RRT) is the most important supportive treatment for acute kidney injury (AKI). Peritoneal dialysis (PD), a relatively safe procedure has been used in pediatric AKI patients. It is the RRT of choice in developing countries. Data in infants and children have shown promising results supporting PD as it provides adequate clearance and correction of metabolic abnormalities even in those who are critically ill. Data from retrospective studies reveal no differences in mortality rates between different modalities of RRT.(51)

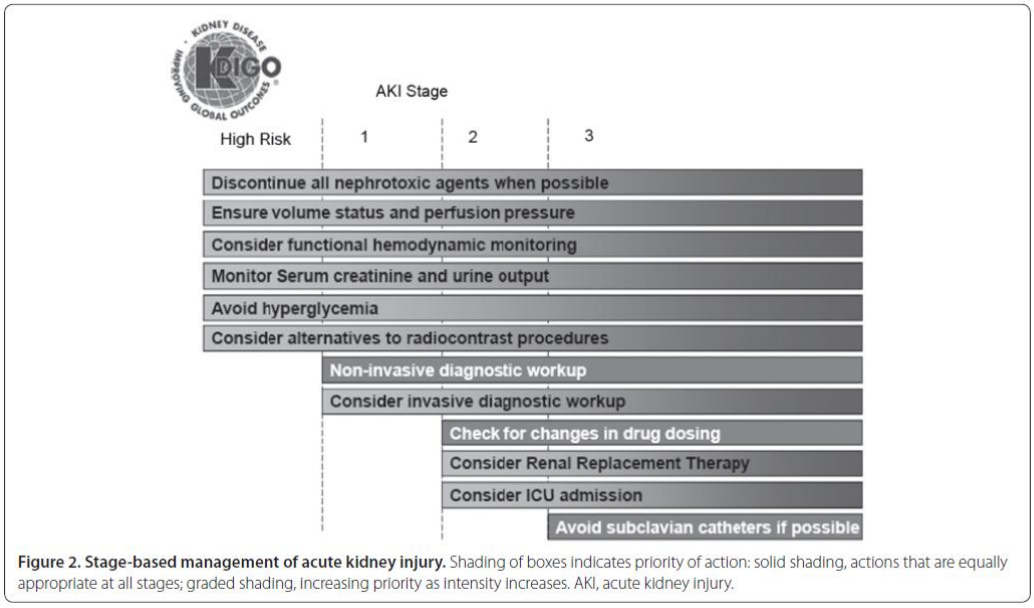


Figure 2. Stage-based management of acute kidney injury. Shading of boxes indicates priority of action: solid shading, actions that are equally appropriate at all stages; graded shading, increasing priority as intensity increases. AKI, acute kidney injury.

Guideline 3 for patients at increased risk for CKD .(49)

To date, no singular effective therapy has been developed to alter its natural history. However, advancements have been made across several fronts including the development of robust and validated tools for clinical risk identification such as the concept of renal angina, discovery of novel damage biomarkers to enable early detection of injury, use of informatics and clinician information systems to modify clinician behavior by providing decision support and harm avoidance, and increased vigilance for long-term surveillance for the sequelae of chronic kidney damage among survivors.(14)

MATERIALS AND METHODS

STUDY DESIGN

This was a prospective observational study conducted under the department of Paediatric Nephrology, Christian Medical College Vellore, Tamil Nadu, India. The location of the study was Paediatric Intensive Care Unit in Christian Medical College Vellore. The study was conducted between the period of March 2017 to July 2017 among the critically ill children admitted in PICU aged 0-15 years after fulfilling the Inclusion criteria. Children who did not fulfill the inclusion criteria were excluded from the study. The parents were informed regarding the purpose of the study and about the nature of the illness by providing the patient information sheet, the consent form, and the informed assent form in different vernacular languages. The clinical research form was filled after obtaining the consent.

INCLUSION CRITERIA:

Critically ill Children aged from 0 to 15 years admitted in Paediatric Intensive Care Unit.

EXCLUSION CRITERIA:

1. Children on Renal Replacement Therapy (Maintenance Dialysis, Peritoneal Dialysis).
2. Chronic Kidney Diseases / Nephrotic Syndrome /Nephritis
3. Post Renal Transplant
4. Children with Pre-existing AKI

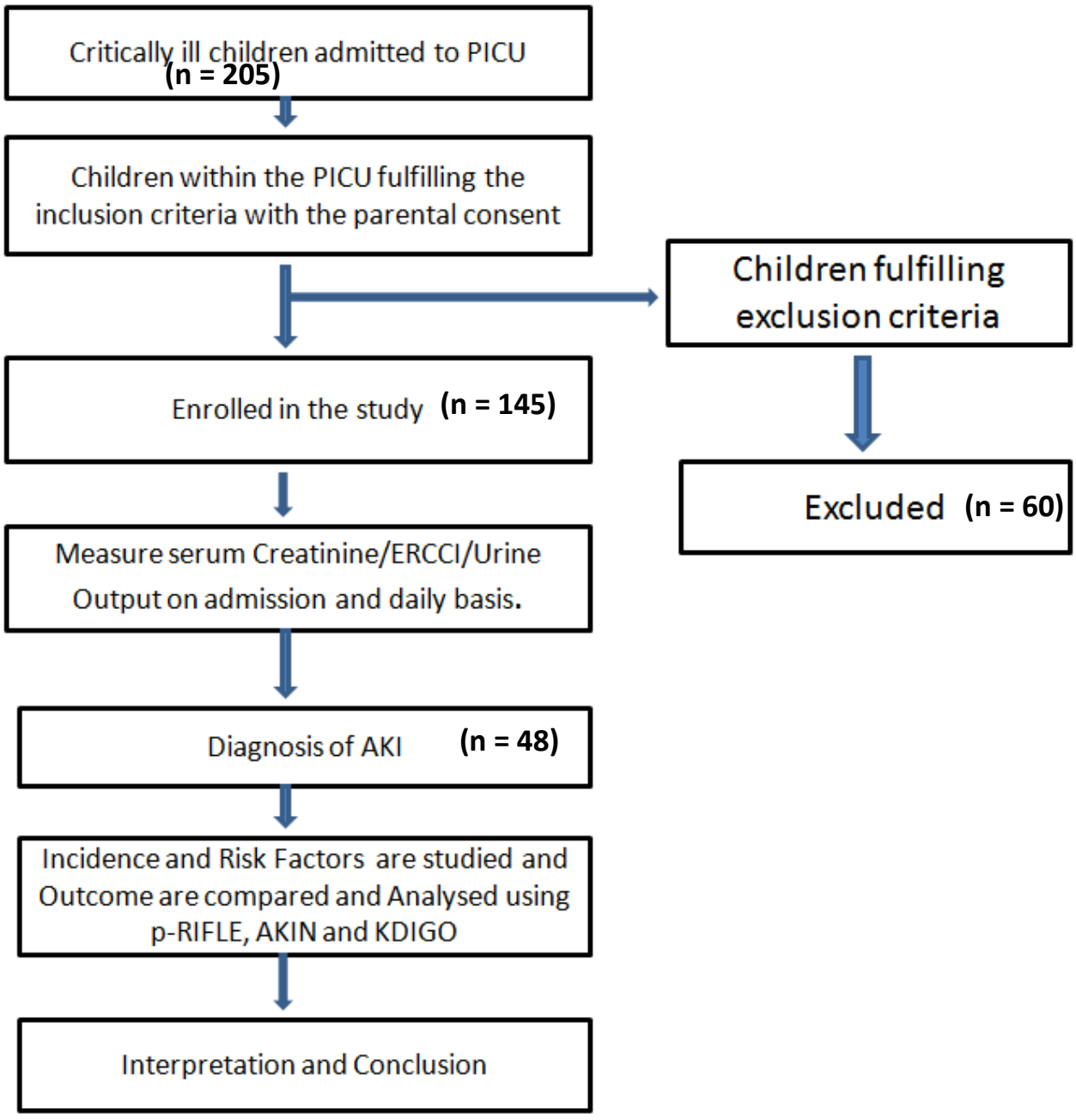
METHODOLOGY:

Serum creatinine was done at admission and on alternate days till 7 days or before discharge whichever is longer. It was analysed by Jaffe method and estimated creatinine clearance (eCC) was calculated as per Modified Schwartz formula. Urine output was measured sixth hourly, in a 24 hour period as per the definitions.

We used serum creatinine,estimated creatinine clearance and urine output to diagnose AKI. Patients were classified as AKI based on rise in serum creatinine or fall in urine output according to Pediatric Risk, Injury, Failure, Loss, End-stage Renal Disease (p-RIFLE), AKIN and KDIGO criteria either at admission or subsequently during the hospital stay; patients who did not develop AKI were served as controls. Baseline creatinine was recorded from the lowest value available in the last three months.If baseline creatinine was not available then serum creatinine was taken as per age appropriate values.

The children with AKI were followed up after discharge to record their recovery from renal failure. They were grouped as per their response into Complete Recovery, Partial Recovery (if improvement in serum creatine, but not normalised) , Acute Kidney Disease (if persistant high creatinine value > 4 weeks) and Dialysis Dependent (if dialysis could not be weaned off). All those who had persistently elevated Serum creatinine were categorized as Acute Kidney Injury Disease.

FLOW CHART- Algorithm of the study



SAMPLE SIZE

Desired Sample size was calculated using the formula **4**[2] to estimate 33.1% the Incidence of Acute Kidney Injury in critically ill children.

$$n = \frac{Z^{2}_{1-\alpha/2}\, p\,(1-p)}{d^{2}}$$

Where,

p : Expected proportion

d : Absolute precision

1- α/2 : Desired Confidence level

Reference for the above formula: Lemeshow S, Hosmer DW, Klar J, Lwanga SK. Adequacy of Sample Size in Health Studies. John Wiley and Sons, 1990.

The sample size was calculated to be 145

STATISTICAL METHOD:

Data entry was done on Epidata and analysis was done using SPSS-17

The incidence of AKI by the three definitions was presented as frequencies and percentages with 95% CI.

The quantitative variables like length of hospital stay, mechanical ventilation, presence of shock were summarized using median with IQR

The categorical variables across the groups were compared using chi-square test.

Logistic regression analysis was used to assess the association of each pRifle, AKIN and KDIGO category with in-hospital mortality.

The discriminative ability of the criteria to correctly predict mortality was assessed by calculating the area under the curve (AUC) of the receiver operating characteristic curve (ROC) likelihood values were obtained from ROC curve. Sensitivity, specificity was presented. The p value of less than 0.05 was considered as significant.

Weighted Kappa was calculated for agreement across the three methods.

RESULTS

RESULTS

This study was conducted in Paediatric Intensive Care Unit from February 2017 to July 2017.

Of the total 205 consecutive admissions, **145 children were enrolled** after fulfilling the Inclusion criteria.

Of these, AKI was diagnosed in 48 children (33.1%) and 97 children (66.9%) were classified as Non AKI.

The demographic details, clinical course and outcome details were noted.

The data collected was statistically analysed.

AGE DISTRIBUTION

TABLE 1

Age (years)	**Frequency (n=145)**	**Percentage (%)**
0-2	54	37.2
2-5	30	20.6
5-10	27	18.6
10-15	34	23.4

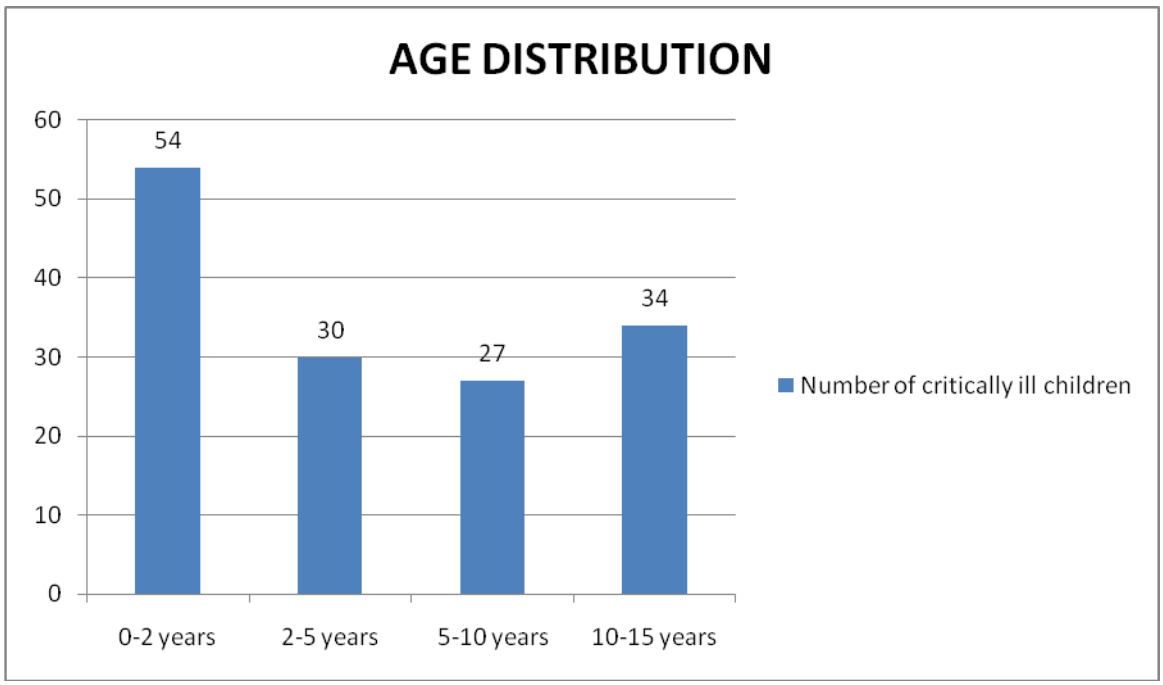


FIGURE 1

The median age of the population studied was 3.4 years (range: 0-15 years).

Majority (37.2) of the children were under 2 years followed by 23.4% in the 10-15 years age group.

The remaining (20.6 %) were between 2-5 years of age and (18.6%) were 5-10 years of age.

GENDER DISTRIBUTION

TABLE 2

Gender	Number (n=145)	Percentage (%)
Male	91	62.75
Female	54	37.24
Total	145	100

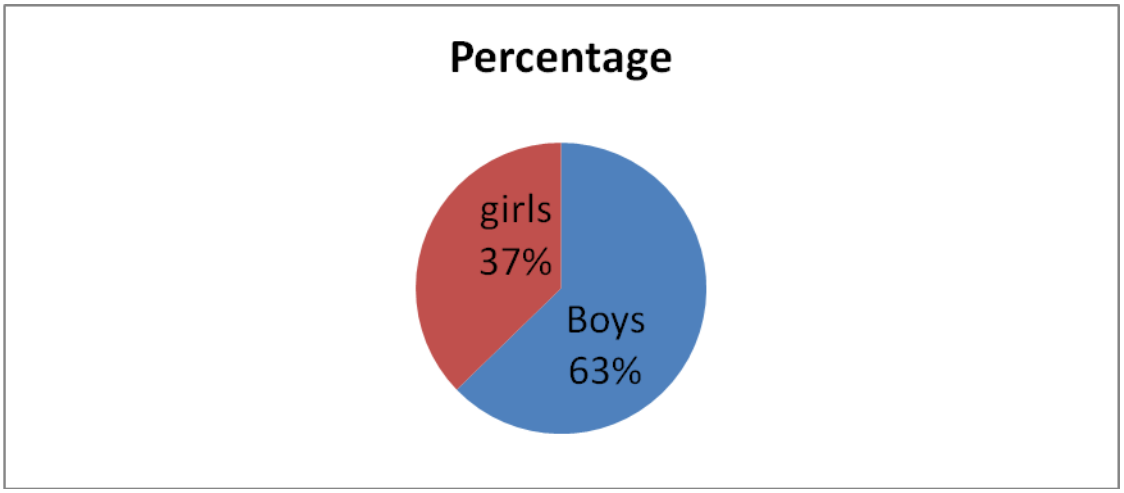


FIGURE 2

There were 62.75 % (91/145) males and 37.24% (54/145) females. The M:F ratio 1.7:1.

ADMISSION DIAGNOSIS AT PRESENTATION

TABLE 3

S No	Diagnosis	Frequency N=145	Percentage %
1	Infections	30/145	20.68
	a. Sepsis	7/30	23.3
	b. Dengue	6/30	20
	c. Pneumonia	5/30	16.6
	d. HLH	4/30	13.3
	e. HIV	2/30	6.6
	f. Diphtheria	2/30	6.6
	g. Salmonella	1/30	3.3
	h. Severe combined immunodeficiency	1/30	3.3
		2/30	6.6
2			
	Neurological	29/145	20
	a. Meningoencephalitis	9/29	31.03
	b. Epilepsy	6/29	20.6
	c. Encephalopathy	4/29	13.7
	d. Cerebral palsy	3/29	10.3
	e. Hydrocephalus	2/29	6.89
	f. CNS HLH	1/29	3.4
	g. Intracranial hemorrhage	1/29	3.4
	h. Head injury	3/29	10.3
3	i.		
	Hematological	19/145	13.1
	a. Leukemia	7/19	36.8
	b. Lymphoma	5/19	26.31
	c. Thalassemia	3/19	15.7
	d. Neuroblastoma	1/19	5.2
	e. Aplastic Anemia	2/19	10.5
4	f. Fanconi's Anemia	1/19	5.2
	g.		
	Respiratory	15/145	10.3
	a. Infectious	7/15	46.67
	b. Non-infectious	8/15	53.3
	- Aspiration pneumonia	1/15	12.5
	- Lipoid pneumonia	1/15	12.5
	- Hydrocarbon ingestion	3/15	20
5	- Pneumothorax	2/15	13.3
	- Bronchial Asthma	1/15	12.5
	-		
	Cardiac	14/145	9.6
	a. Acyanotic heart disease	6/14	42.8
6	b. Cyanotic heart disease	5/14	35.7
	c. Myocarditis	2/14	14.2
	d. Infective endocarditis	1/14	7.1

7	Metabolic	10/145	6.8
8	Diabetic ketoacidosis	4/145	2.7
9	Surgical	4/145	2.7
10	Snake bite	4/145	2.7
11	Drowning	3/145	2.06
12	Hepatic encephalopathy	3/145	2.06
13	Miscellaneous	10/145	6.89

The most common diagnosis at admission to PICU was infections (20.68 %) and neurological disorders (20%), followed by hematological causes (13.1%)

Respiratory- 10.3%, cardiac 9.65%and metabolic 6.89% were the remaining.

INTERVENTIONS IN PICU

TABLE 4

Parameters	Yes/No	Frequency	Percentage %
Shock (n=145)	Yes	76	52.4
	No	69	47.6
Inotropes (n=145)	Yes	83	57.2
	No	62	42.8
Mechanical ventilation (n=145)	Yes	96	66.2
	No	49	33.8

Among the 145 critically ill children, 76 (52.4%) were treated for shock with fluid boluses, 57.2% required inotropes and 66.2% required mechanical ventilation

LENGTH OF PICU STAY:

TABLE 5

Length of stay (Days)	Frequency (number)	Percentage %
0-3	39	26.9
4-7	63	43.4
8-14	26	17.9
15-30	17	11.7

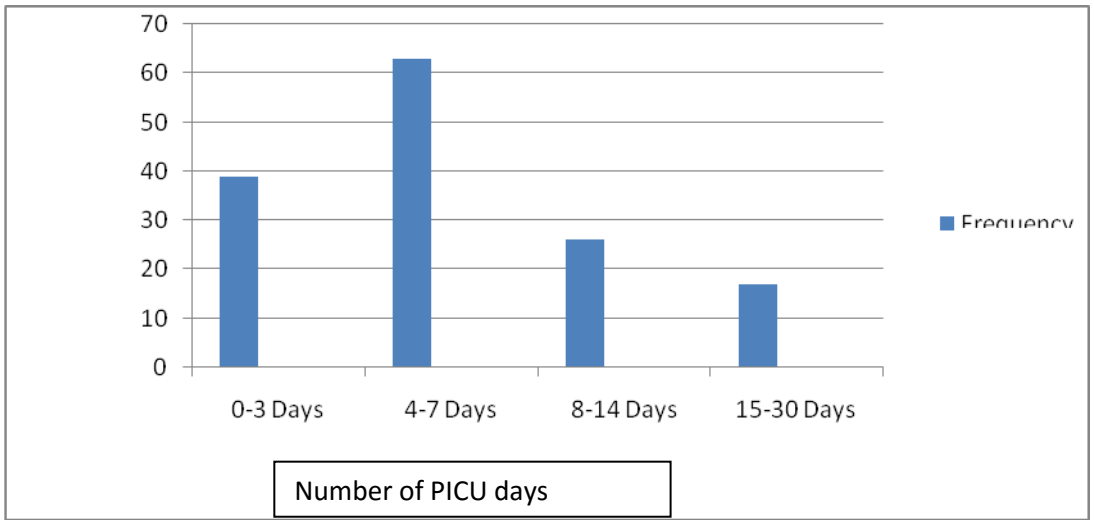


FIGURE 3

The median Length of stay of children in PICU was 5 days with interquartile range (IQR) of 3 to 9 days.

PART II

Of the total 145 children, 48 children had AKI which was diagnosed based on rising serum creatinine or fall in urine output according to the definitions proposed by ADQI.

The clinical characteristics of those with AKI and without AKI were compared.

INCIDENCE OF AKI IN PICU

TABLE 6

Critically ill children	Frequency (n = 145)	Percentage (%)
AKI	48	33.1
Non- AKI	97	66.9

The incidence of AKI in the study population was 33.1% (48/145)

AGE DISTRIBUTION WITH AKI

TABLE 7

Age	AKI	
	Number	**Percentage**
0-2	8	13.8
2-5	13	44.8
5-10	7	28
10-15	20	60.6
Total	48	33.1

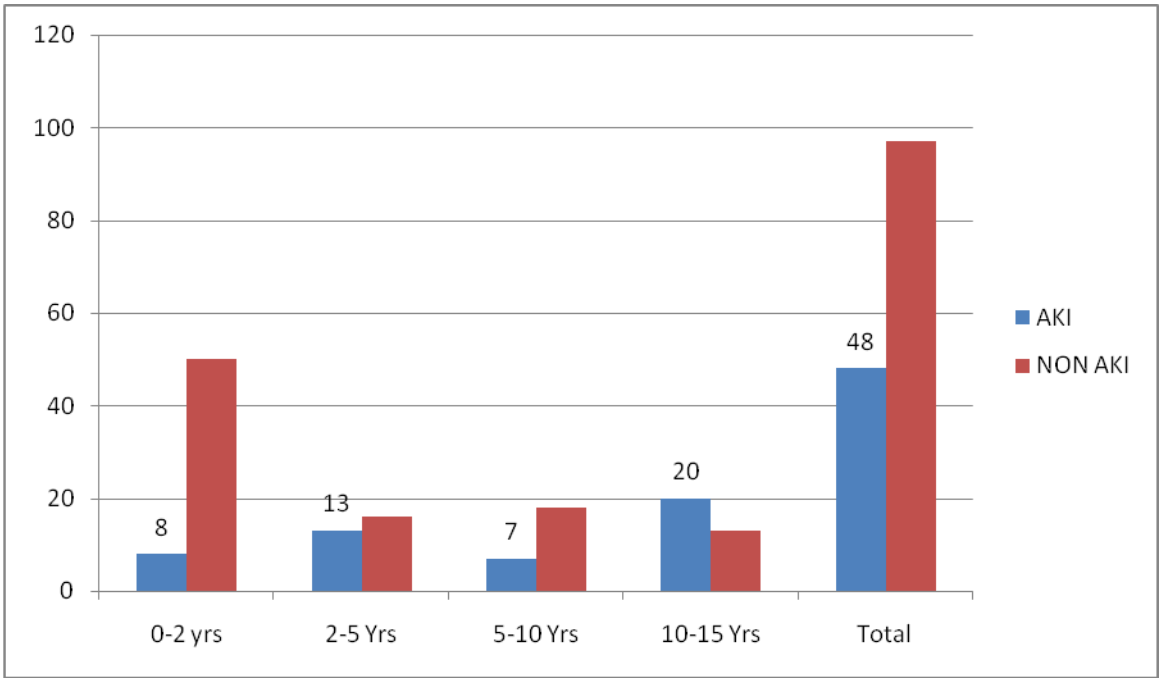


FIGURE 4

The median age group was 6.75 years with the IQR of 3 to 12 years

Among the 48 children, AKI was predominantly seen in the age group of 10 to 15 (60.6%) years followed by 2-5 years (44.8%) and was least in the age group of 5 – 10 years (13.8%)

GENDER DISTRIBUTION – AKI

TABLE 8

GENDER	AKI	
	N	**%**
Male (n=91)	27	56.25
Female (n=54)	21	43.75
TOTAL	48	100

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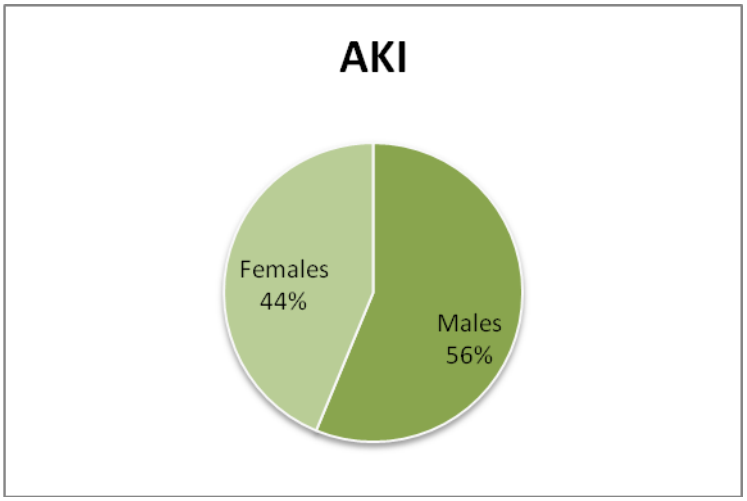

FIGURE 5

Among the children with AKI, 27 were Males and 21 were Females.

Male to Female ratio was 1.28:1.

DIAGNOSES OF CHILDREN WITH AKI
TABLE 9

S.No	Diagnosis	Frequency N=48	Percentage %
1	**INFECTIONS**	**14/48**	**29.1**
	• Probable sepsis • Diptheria • MRSA • Serratia • SCID • Dengue	8/14 2/14 1/14 1/14 1/14 1/14	57.14 14.2 7.1. 7.1 7.1 7.1
2	**NEUROLOGICAL**	**9/48**	**18.75**
	• Meningoencephalitis • • Encephalopathy • Epilepsy • Global developmental delay • Autoimmune encephalitis	3/9 2/9 2/9 1/9 1/9	33.3 22.2 22.2 11.1 11.1
3	RESPIRATORY	6/48	12.5
	Hydrocarbon ingestion	3/6	50
	H1N1 Pneumonia	2/6	33.3
	Pneumothorax	1/6	16.6
4	**HAEMATOLOGICAL**	**5/48**	**10.4**
	Leukemia- T cell and B cell	3/5	60.0
5	**Diabetic ketoacidosis**	**3/48**	**6.25**

6	**Meytabolic**	**2/48**	**4.1**
7	**Cardiac**	**1/48**	**2.08**
8	**Surgical**	**1/48**	**2.08**
9	**Hepatic**	**1/48**	**2.08**
10	**Drowning**	**1/48**	**2.08**
11	**Miscellaneous**	**5/48**	**10.4**

Amongst the children diagnosed with AKI Infections (29.1%) remained the predominant condition followed by neurological (18.75), hematological (10.4), respiratory (12.5) and other miscellaneous causes.

Amongst the infections, most common was Probable sepsis in 57.14% followed by Hydrocarbon ingestion in 50 % (Respiratory causes), Leukemia in 60% with hematological causes, 18.75% had Meningo-encephalitis amongst neurological causes and 6.25% had DKA.

DIAGNOSIS OF AKI BASED ON DEFINITIONS

The children admitted in PICU were also classified as AKI - based on the three criteria proposed by ADQI. These included serum creatinine and urine output.

These criteria were pRIFLE, AKIN and KDIGO.

All three of them had three stages I, II, and III (Risk, Injury and Failure) but with some variances.

These three criteria were further compared for their aggreability.

An attempt was made to assess which of the three criteria could best diagnose AKI and predict its outcome.

TABLE 10

Definitions	**pRIFLE**			**AKIN**			**KDIGO**		
Staging	**Stage I**	**Stage II**	**Stage III**	**Stage I**	**Stage II**	**Stage III**	**Stage I**	**Stage II**	**Stage III**
Number	**23**	**6**	**19**	**24**	**5**	**18**	**22**	**4**	**21**
Percentage	**48**	**12**	**39.5**	**51.06**	**10.63**	**38.30**	**46.80**	**8.51**	**44.69**

INCIDENCE OF AKI BASED ON SERUM CREATININE

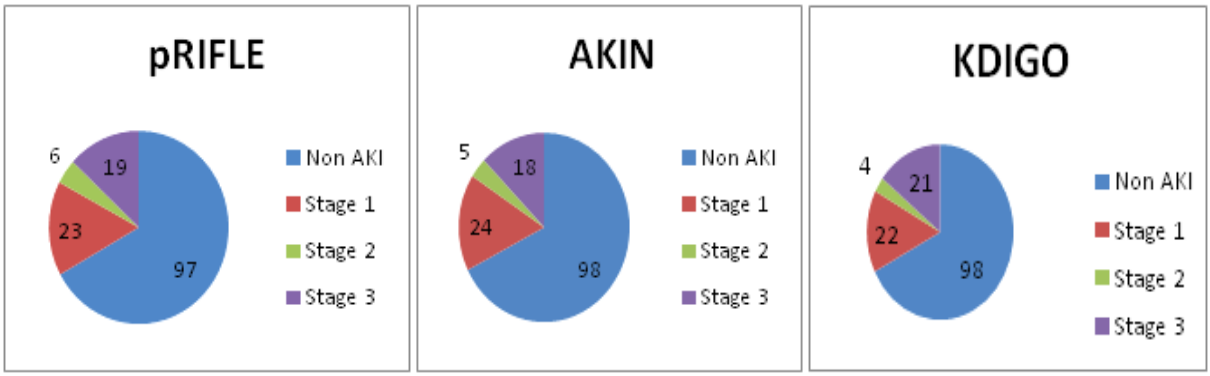

FIGURE 6

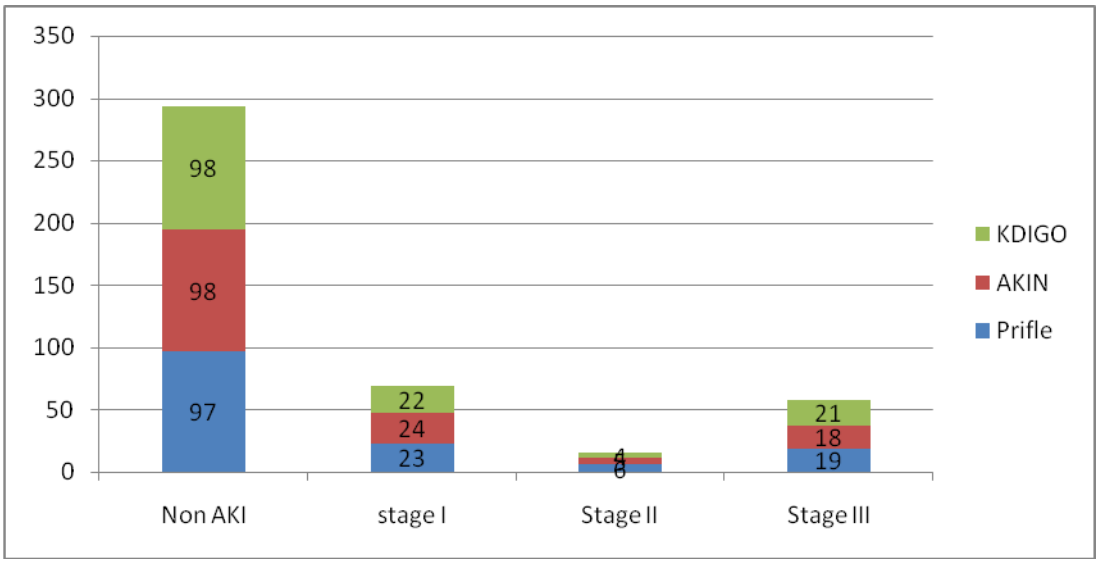

FIGURE 6

Using p RIFLE, 48 were diagnosed as AKI .Of these 23 were in stage 1, 6 in stage 2 and 19 in stage 3.

Using AKIN, 47 were diagnosed as AKI .Of these 24 were in stage 1, 5 in stage 2 and 18 in stage 3

Using KDIGO, 47 were diagnosed as AKI .Of these 22 were in stage 1, 4 in stage 2 and 21 in stage 3**.**

The three criteria appeared to be almost comparable

INCIDENCE OF AKI BASED ON URINE OUTPUT:

TABLE 11

Definitions	pRIFLE			AKIN			KDIGO		
Staging	**Stage I**	**Stage II**	**Stage III**	**Stage I**	**Stage II**	**Stage III**	**Stage I**	**Stage II**	**Stage III**
Number	**6**	**3**	**3**	**6**	**3**	**2**	**7**	**2**	**3**

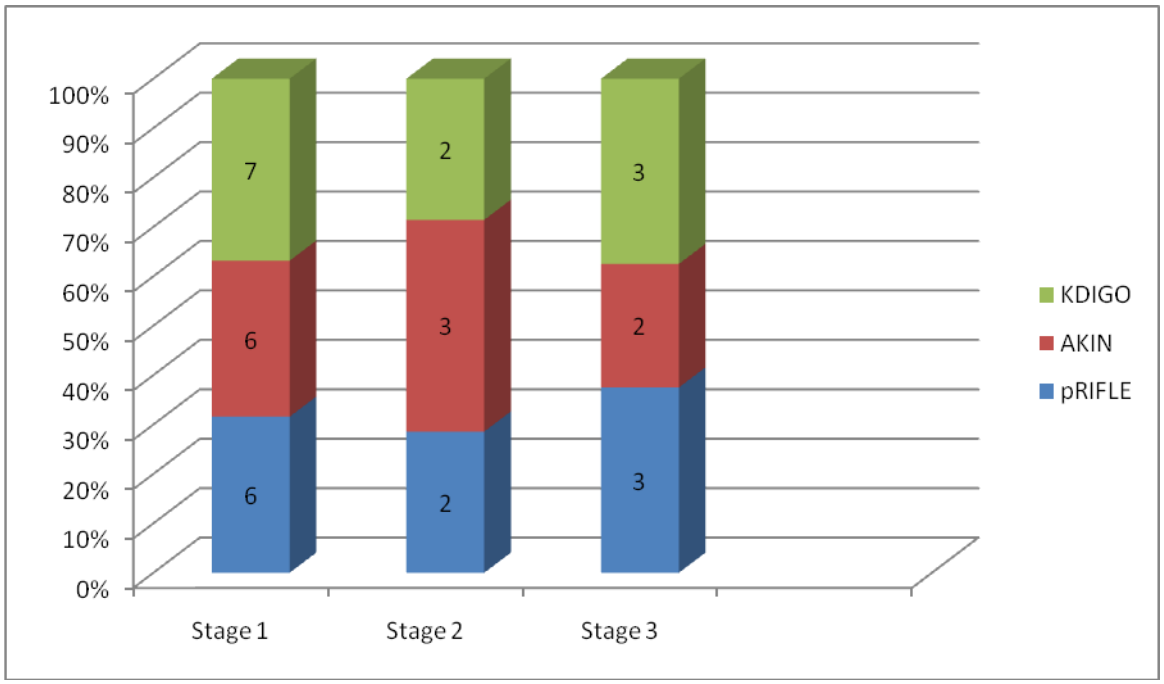

FIGURE 7

pRIFLE- of total 11 children had AKI of which 6 in stage I, 2 in stage II and 3 in stage III,

AKIN - of total 11 had AKI - 11, of which 6 were in stage I, 3 as stage II and 2 as stage III

KDIGO- of the total 12, 7 were in stage I, 2 in stage II and 3 in stage III.

RISK FACTORS AND INTERVENTIONS IN THOSE WITH AKI

TABLE 12

Parameters	Yes/No		Frequency	Percentage %	P Value
Shock (n=48)	Yes		29	60.4	P =<.05
	No		19	39.6	
Inotropes (n=48)	Yes		35	72.9	**P=<0.01**
	No		13	27.1	
Mechanical ventilation (n=48)	Yes	<72hrs	11	22.9	**P=<0.001**
		>72hrs	28	58.5	
	No		9	18.8	

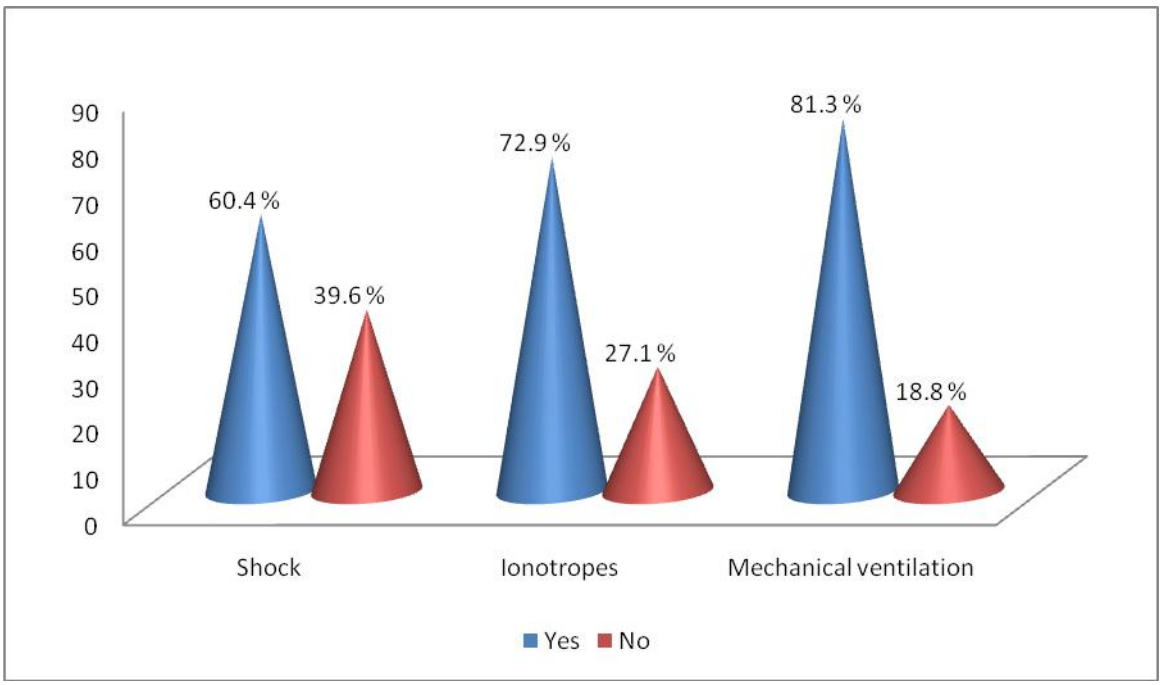

FIGURE 8

In the present study, of the 48 children with AKI, 60.4% (n= 29) had a risk factor of shock.

Of the total, 72.9% (n = 35) were treated with inotropes and 81.3% (n= 39) required mechanical ventilation

Blood support was required in as many as 66.8%; while nephrotoxic medications were administered in only 2.06% children.

The occurrence of shock, use of inotropic support, and Ventilation had a highly significant (p= <0.01) association with the risk of developing AKI.

DURATION OFF MECHANICAL VENTILATION:

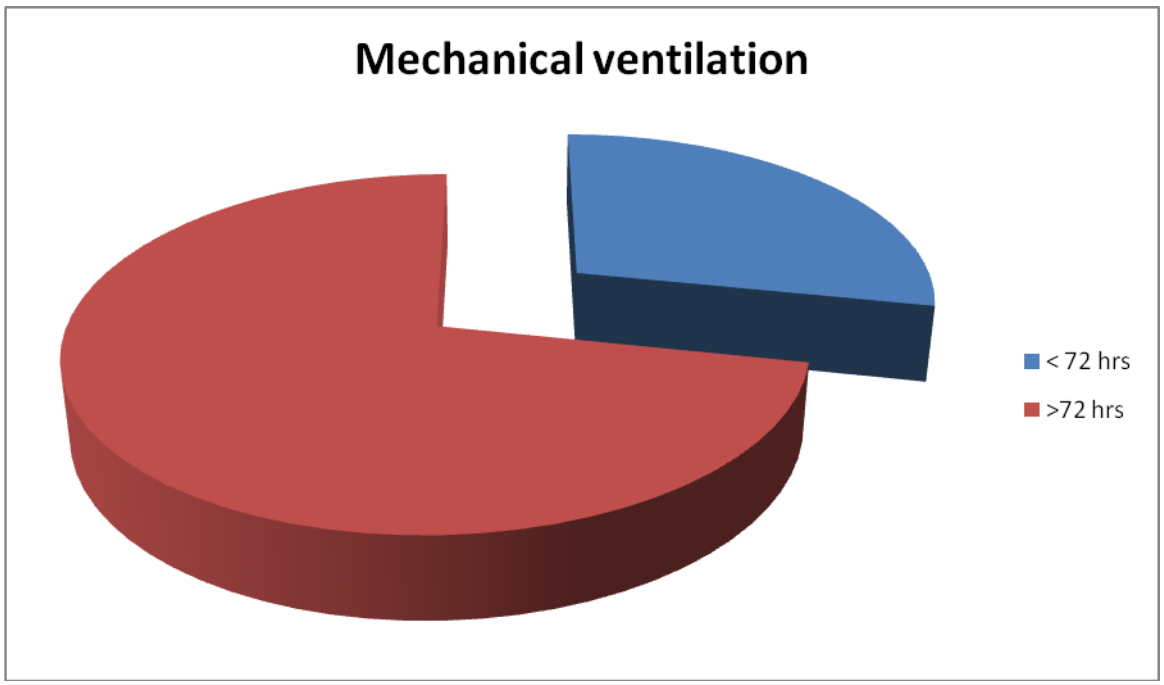

FIGURE 9

Among the mechanically ventilated children, 28.2% (n= 11) were ventilated for <72 hours and rest were ventilated for >72 hours.

There was a significant association between the duration of mechanical ventilation (>72 hours) and those with (< 72hours) **(p<0.001)**

RENAL REPLACEMENT THERAPY

TABLE 13

	RENAL REPLACEMENT THERAPY				TOTAL	
	YES		NO			
	n	%	n	%	n	%
AKI	**14**	**29.17**	**34**	**70.83%**	**48**	**100**

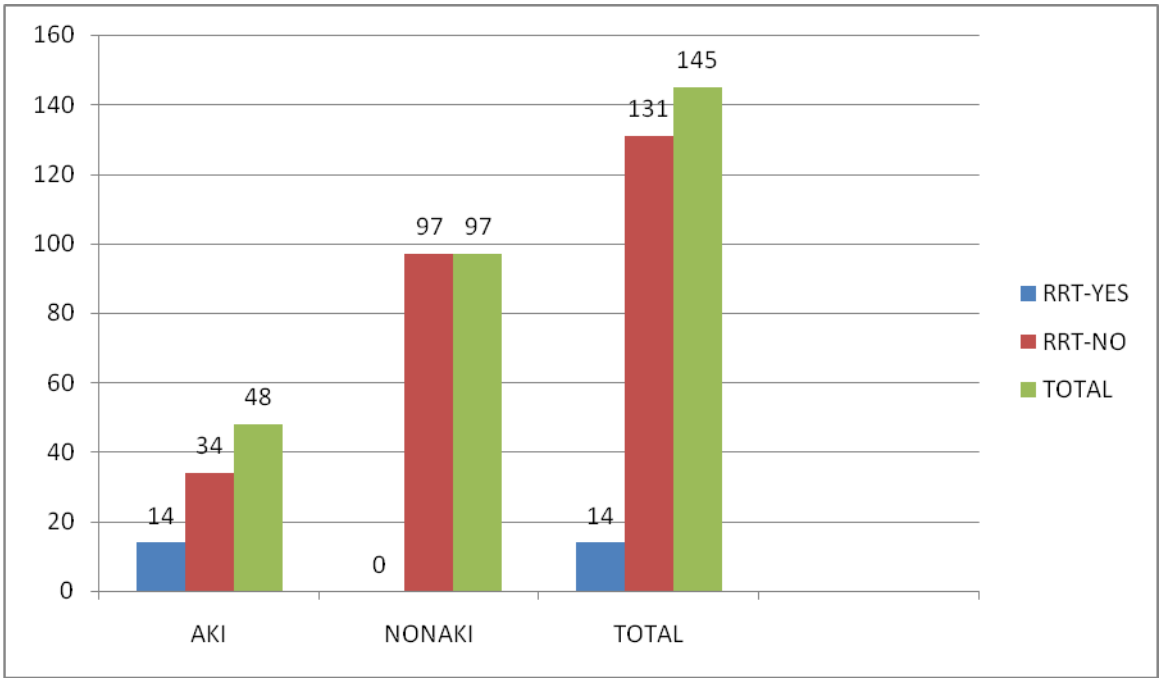

FIGURE 10

Of the 48 children who had AKI, 14 required Renal Replacement Therapy (29.17%)

Taking the group as a whole, out of 145 critically ill children 9.7% (n=14) required RRT

TYPES OF RENAL REPLACEMENT THERAPY

TABLE 14

Renal Replacement therapy	AKI (n=48)	NON-AKI
NIL	34	97
Peritoneal dialysis	10/48	00
Hemodialysis	04	00
Total	48	97

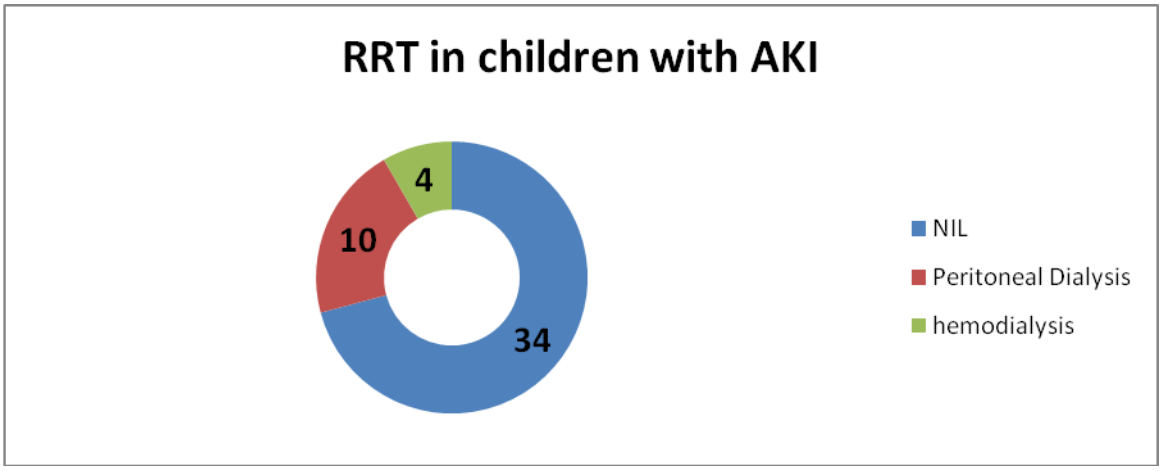

FIGURE 11

Out of 48 children with AKI, 14/48 (29.1 %) required Dialysis.

Of these, Peritoneal dialysis was done in 10 /14 (71.4%) and Hemodialysis in 4 /14 (28.5%) The remaining **34** did not require RRT

OVERALL OUTCOME IN PICU

TABLE 15

Outcome	Number	Percentage %
Discharge	95	65.5
DAMA	20	13.7
Death	30	20.6
Total	145	100

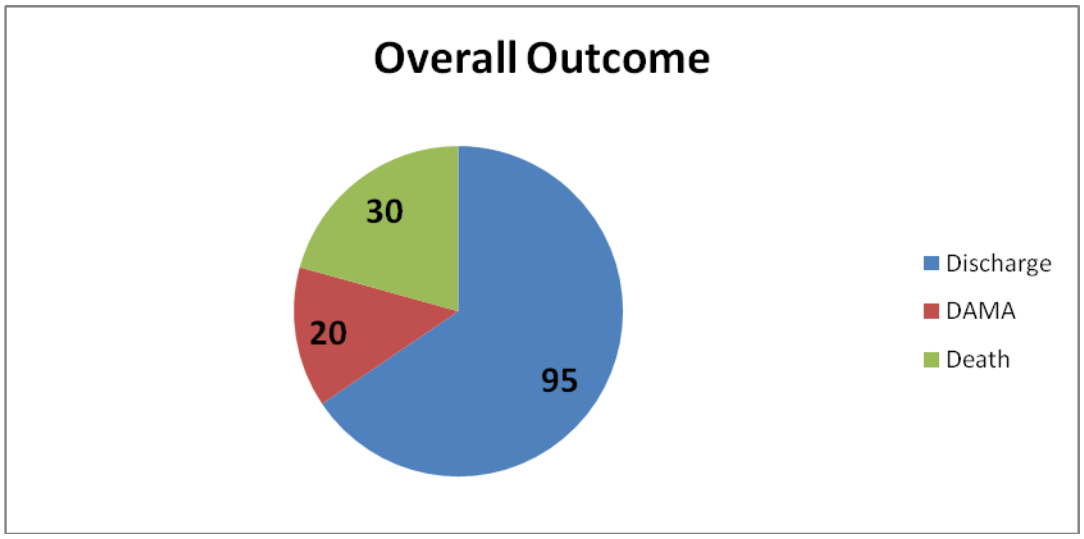

FIGURE 12

The number of children discharged well were 95/145 (65.5%),

The number of children who died (30/145= 20.65) along with those who were Discharged Against Medical Advice 20 (13.7%) and presumed to have an **adverse outcome were 34.35%**

OVERALL OUTCOME BETWEEN AKI AND NON AKI

TABLE 16

	OVERALL OUTCOME						TOTAL	
	DISCHARGED N=95		DEATH N=30		DAMA N=20			
	n	%	n	%	N	%	n	%
AKI n=48	28/48	58.3	14/48	29.1	6/48	12.5%		100
NON AKI n=97	67/95	70.5	16/30	53.3	14/20	70	145	100
TOTAL	95	65.5	30	20.7	20	13.8	145	100

OUTCOME BETWEEN AKI AND NON AKI

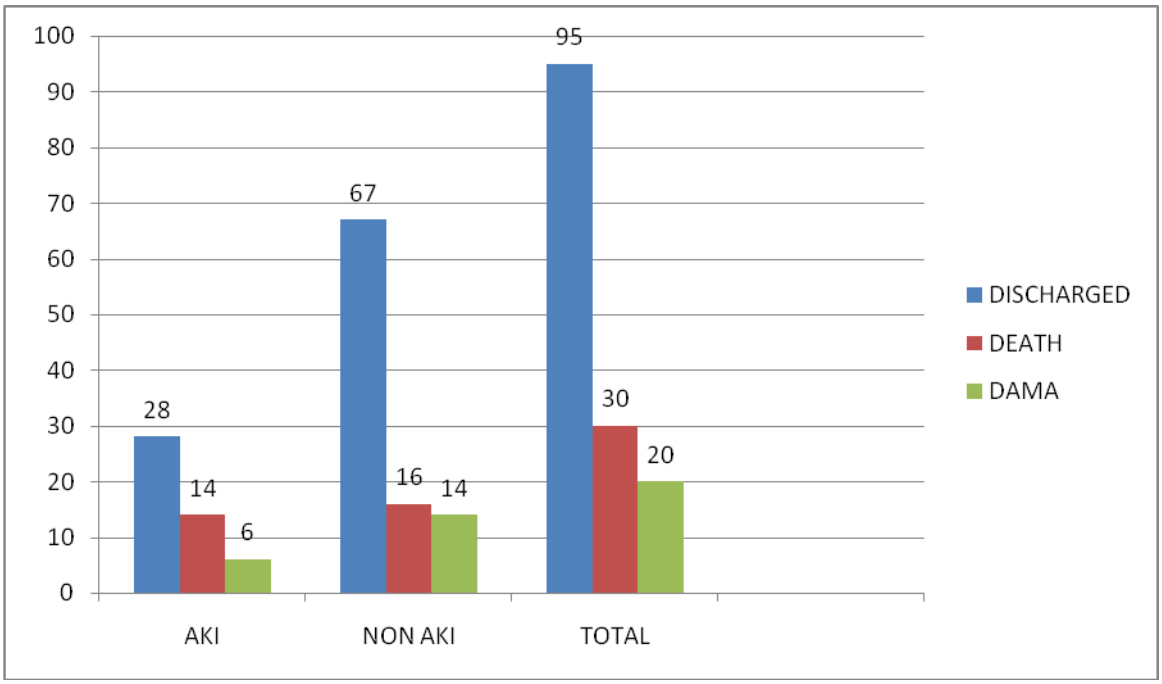

FIGURE 13

Among the children with AKI, 28 (58.3 %) had complete recovery, 14 died (29.2%) and 6 (12.5%) were Discharged against medical Advice.

Amongst those discharged, 29.5% had AKI and 70.5 % were non AKI

Amongst those who died, 46.6% had AKI and 53.3% were non AKI

Amongst those who went on DAMA-30% had AKI and 70% were non AKI

RENAL OUTCOME IN AKI

TABLE 17

AKI N=48	**RENAL OUTCOME**								**TOTAL**	
	IMPROVED N		**PARTIALLY IMPROVED**		**AKD**		**DIALYSIS DEPENDENT**			
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
YES	32	66.6	5	10.4	9	18.8	2	4.2	48	100

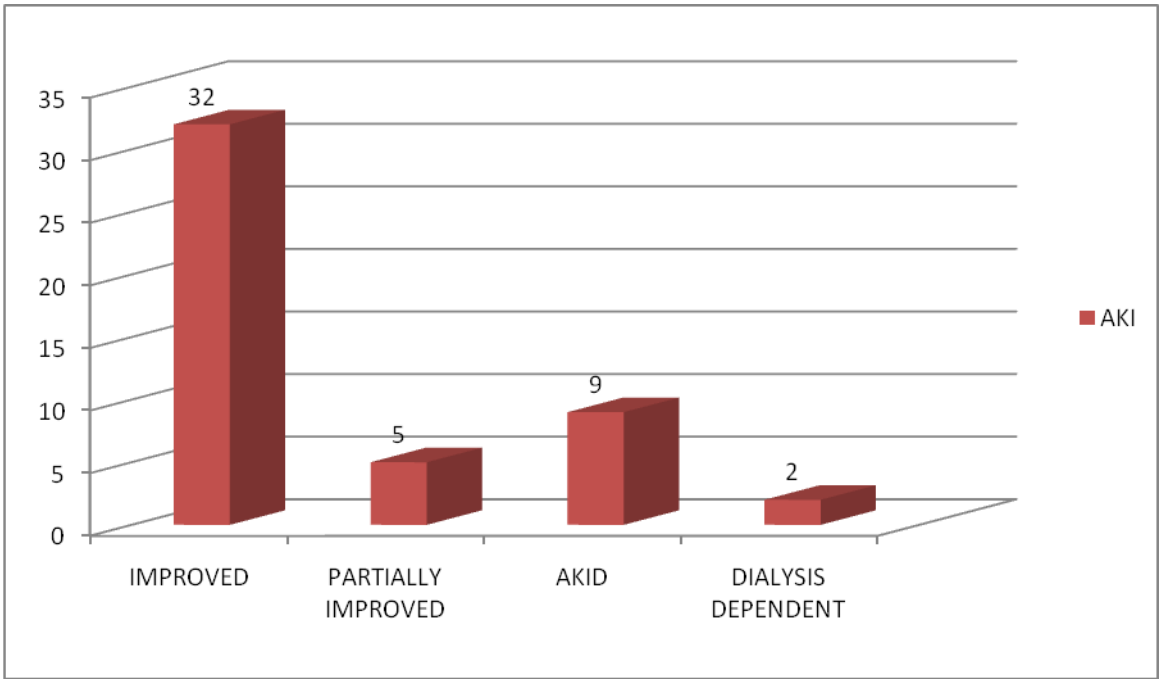

FIGURE 14

Of the 48 children with AKI, 66.66% (32/48) improved completely

10.4% (n=5) partially improved

18.8% (n= 9) developed Acute Kidney Injury disease

4.2% (n= 2) became dialysis dependent.

Renal outcome was significantly poorer in children with AKI than Non AKI children (p=<0.001).

LENGTH OF PICU STAY

TABLE 18

Definitions	Stage	Length of PICU stay (days)
pRIFLE	Stage 1	13
	Stage 2	7
	Stage 3	8
AKIN	Stage 1	11
	Stage 2	6
	Stage 3	8
KDIGO	Stage 1	11
	Stage 2	6.5
	Stage 3	8

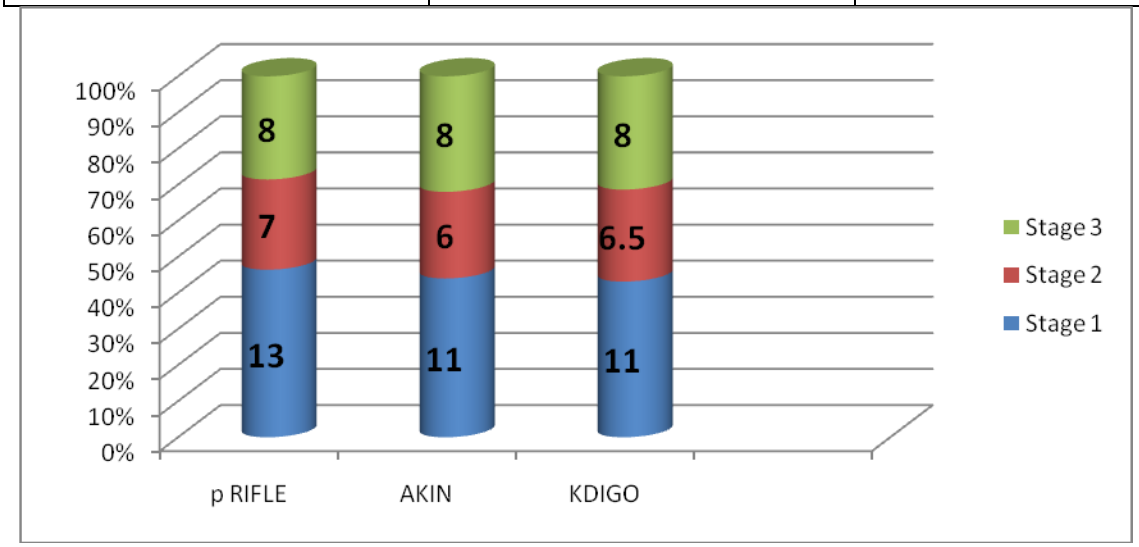

FIGURE 15

The median length of stay of children with AKI in PICU was found to be 7 days with an IQR of 3.5 days to 12 days.

There was **no significant difference** between the **Length of stay** of children **with AKI** based on the different criteria.(p=>0.05)

INTER DEFINITION AGREEMENT

TABLE 19

Stages	AKI		
	p-Rifle	AKIN	KDIGO
Stage 1	22/48	24/47	22/47
Stage 2	5/48	5/47	4/47
Stage 3	21/48	18/47	21/47

All the three definitions were in Agreement with regard to diagnosis of AKI (Weighted kappa)

AKIN VS KDIGO K 0.889 P= <0.001

AKIN VS pRIFLE K 0.918 P= <0.001

pRIFLE VS KDIGO k 0.945 P =<0.001

STAGE WISE RENAL OUTCOME-pRIFLE

TABLE 20

Stage	Improved	Partially Improved	AKD	Dialysis Dependent	Total
Stage 1	8	1	0	0	9
Stage 2	13	2	1	1	17
Stage 3	11	2	8	1	22
Total	32	5	9	2	48

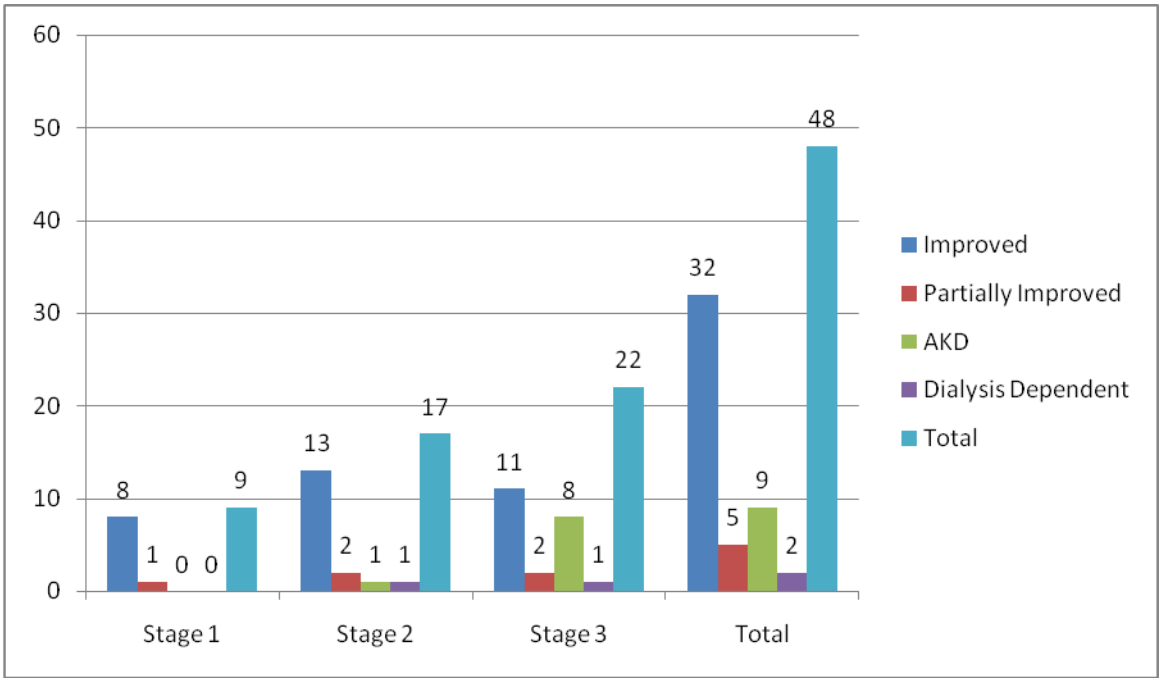

FIGURE 16

Of the total children, 2 became dialysis dependent and 9 developed AKI

Of the dialysis dependent, one was diagnosed in stage 2 and 1 in stage 3.

Of the total, 8/22 (36.365) developed Acute Kidney Injury Disease (8/22) and were diagnosed in stage 3.

STAGE WISE <u>OVERALL OUTCOME</u> WITH p-RIFLE

TABLE 21

Stage	Overall outcome			Total
	Discharged	Death	DAMA	
Stage 1	6	1	2	9
Stage 2	11	3	3	17
Stage 3	11	10	1	22
Total	28	14	6	48

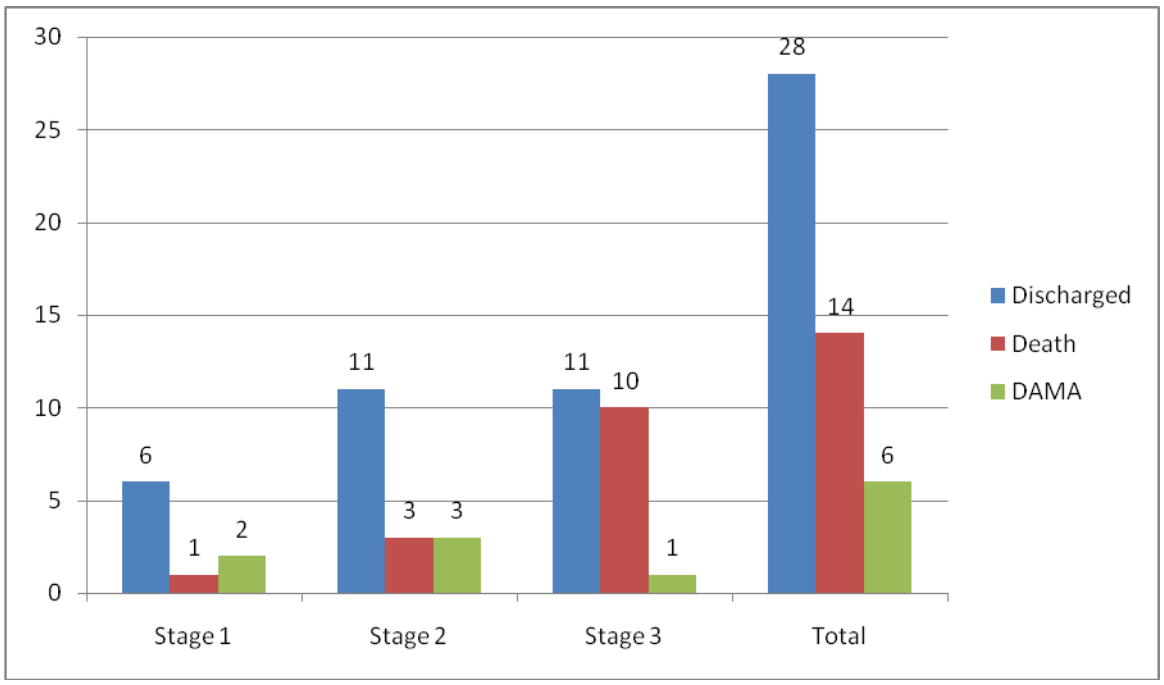

FIGURE 17

With p-RIFLE more critically ill children succumbed to death in stage 3 – 45.45% (10/22) as against 1/9 (11.11%) in stage 1 and 3/17 (17.6) in stage 2.

Discharge Against Medical Advice occurred in both stage 2 and 3.

STAGE WISE RENAL OUTCOME WITH AKIN

TABLE 22

Stage	Improved	Partially Improved	AKID	Dialysis Dependent	Total
Stage 1	17	1	0	0	18
Stage 2	4	1	3	1	9
Stage 3	11	2	6	1	20
Total	32	4	9	2	47

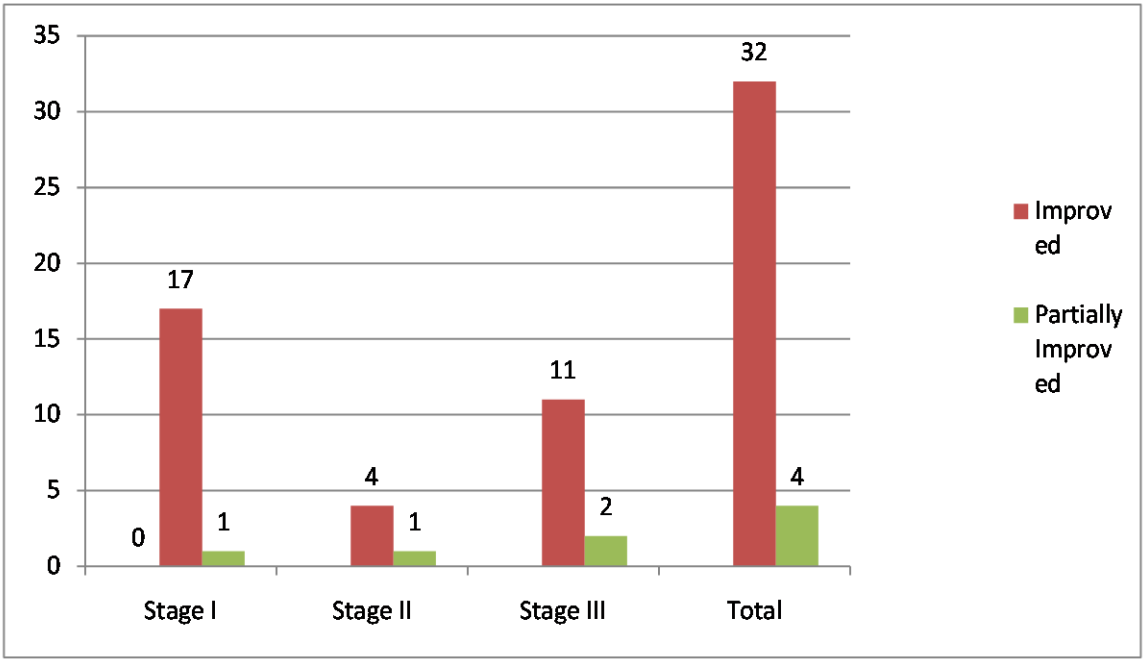

FIGURE 18

Majority of critically ill children improved with Stage 1 AKI (17/18)

Most children who developed AKD were in AKIN Stage 2 (3/9- 33.3%) and Stage 3 (6/20- 30%) at the time of diagnosis

OVERALL OUTCOME - AKIN

TABLE 23

Stage	Overall outcome			Total
	Discharged	Death	DAMA	
Stage 1	12	2	4	18
Stage 2	4	4	1	9
Stage 3	11	8	1	20
Total	27	14	6	47

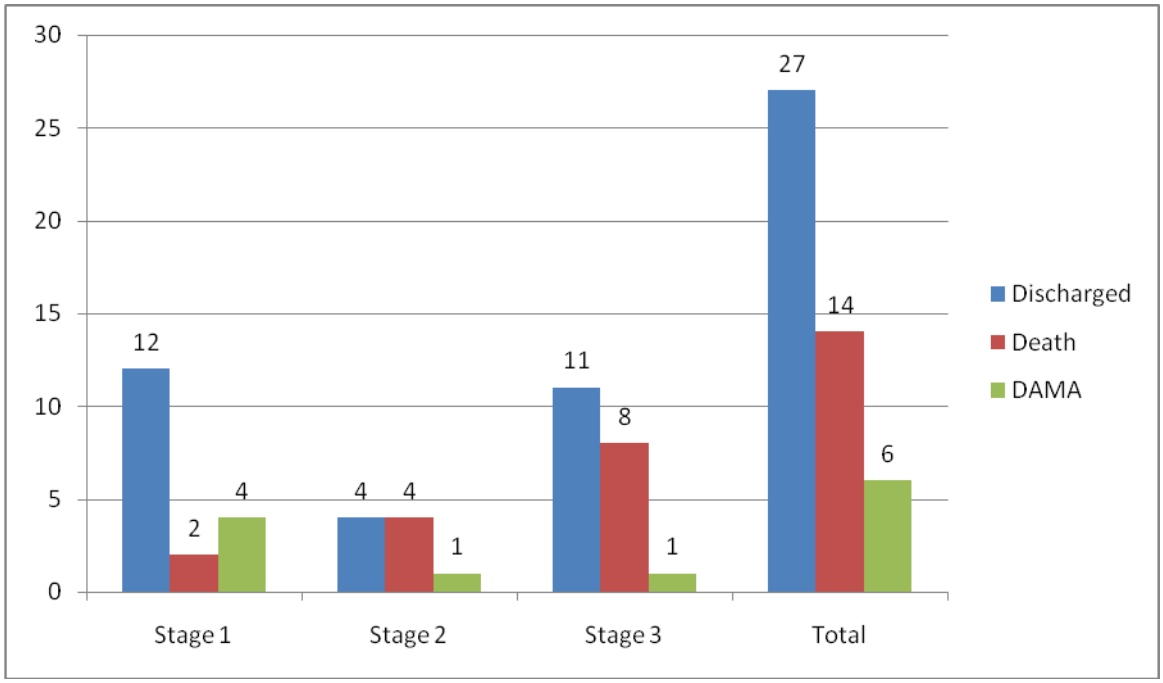

FIGURE 19

Critically ill children with AKI in this study had a better outcome in the stage 1 (12/18)

Mortality was higher in those with Stage 3 -8/20 (40 %).

Risk of death in stage 1 was 2/18 (11.1%) and in stage 2 was 4/9 (44.4%)

STAGE WISE RENAL OUTCOME- KDIGO

TABLE 24

Stage	Improved	Partially Improved	AKID	Dialysis Dependent	Total
Stage 1	14	2	1	0	17
Stage 2	6	2	3	1	12
Stage 3	10	2	5	1	18
Total	30	6	9	2	47

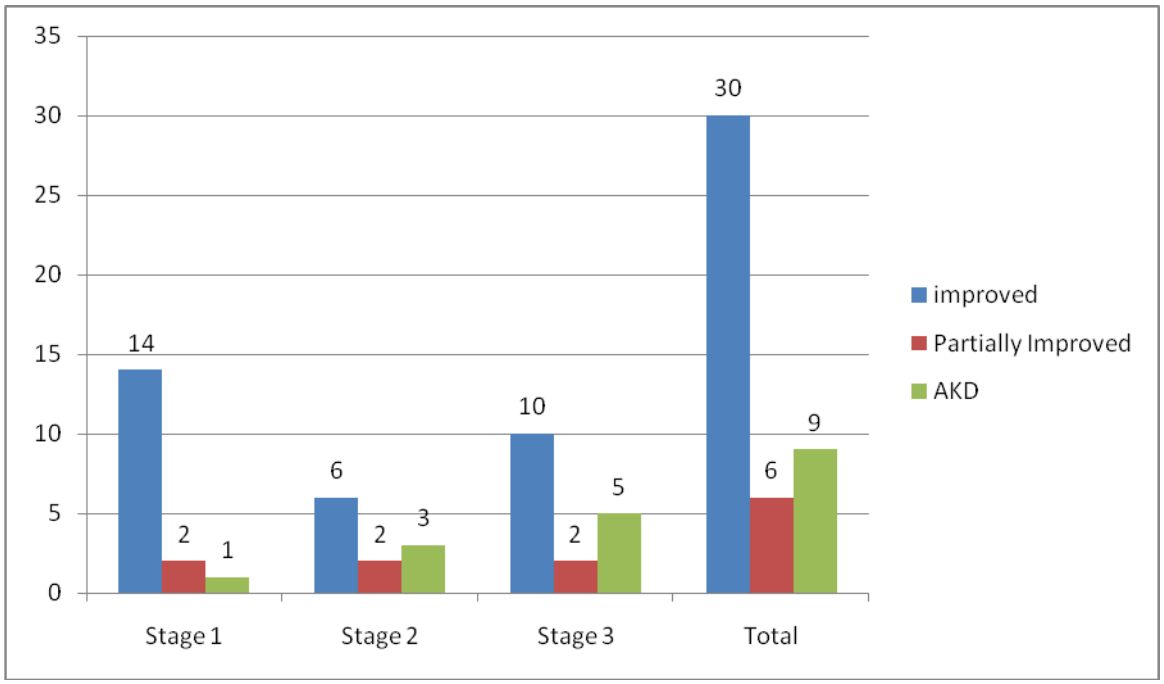

FIGURE 20

Improvement in the Renal status was seen in (13/15-86.6%) in patients in Stage I AKI .

AKID developed in 3/12 -25% in patients in stage 2 and 5/18 – 27.77% in stage 3 AKI

OVERALL OUTCOME - KDIGO

TABLE 25

Stage	Overall outcome N= 45			Total
	Discharged	Death	DAMA	
Stage 1	11	2	4	17
Stage 2	6	5	1	12
Stage 3	10	7	1	18
Total	27	14	6	47

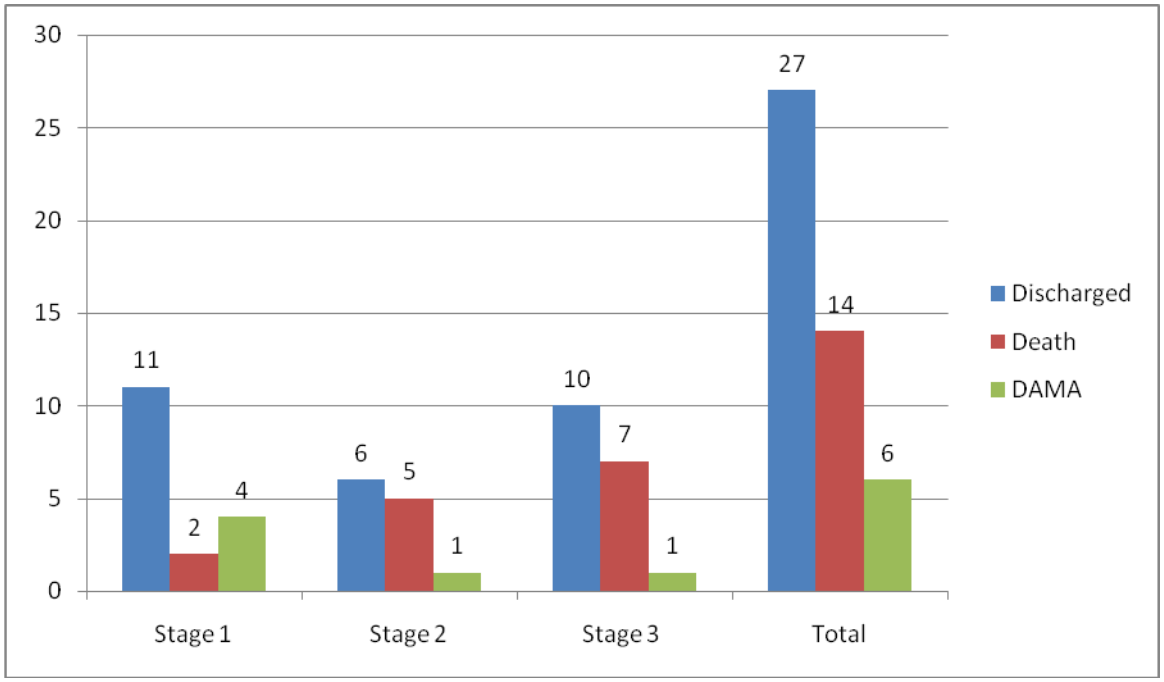

FIGURE 21

The mortality was highest in those in stage 3 (7/18-38.8%), followed by those in stage 2 (5/12-41.6%). Death in stage 1 was only 2/15 (13.3%)

AKI CRITERIA AND MORTALITY

TABLE 26

Stage	Overall mortality	DAMA	Mortality in stage III	P value
pRIFLE	**14**	**6**	**10/48 - (20.80%)**	**0.023**
AKIN	14	6	8/47 - (17.02 %)	0.183
KDIGO	14	6	7/47 - (14.80%)	0.299

pRIFLE was the best predictor of mortality amongst stage 3 patients when compared to AKIN and KDIGO.This was statistically significant (p- <0.000)

COMPARISON OF AGREEMENT BETWEEN CRITERIA

TABLE 27

Agreement between p-RIFLE and AKIN based on Serum Creatinine

Serum Creatinine p-RIFLE	Serum Creatinine AKIN				
	NIL	Stage 1	Stage 2	Stage 3	Total
NIL	80 (55.17%)	0	0	0	80 (55.17%)
Risk /Stage 1	02 (1.38%)	19 (13.1%)	0	0	21 (14.48%)
Injury /Stage 2	01 (.69%)	11 (7.59%)	06 (4.14%)	02 (1.38%)	20 (13.79%)
Failure/Stage3	0	03 (2.07%)	04 (2.76%)	17 (11.72%)	24 (16.55%)
Total	83 (57.24%)	33 (22.76%)	10 (6.90%)	19 (13.10%)	145 (100%)

The correlation between **AKIN Versus p-RIFLE** based on serum creatinine in diagnosing **AKI** showed **Best agreement** in stage I, **but it was not the best**

Out of 21 Stage 1 patients under pRIFLE, 19 agreed with AKIN.

Out of 20 Stage 2 patients under pRIFLE, 6 agreed with AKIN

Out of 24 Stage 3 patients under pRIFLE, 17 agreed with AKIN

TABLE 28

Agreement between p-RIFLE and KDIGO based on Serum Creatinine					
Serum Creatinine (p-RIFLE)	Serum Creatinine KDIGO				
	NIL	Stage 1	Stage 2	Stage 3	Total
NIL	80 (55.17%)	0	0	0	80 (55.17%)
Stage 1	05 (3.45%)	14 (9.66%)	01 (0.69%)	01 (0.69%)	21 (14.48%)
Stage 2	03 (2.07%)	10 (6.90%)	06 (4.14%)	01 (0.69%)	20 (13.79%)
Stage 3	00	04 (2.76%)	04 (2.76%)	16 (11.03%)	24 (16.55%)
Total	88 (60.69%)	28 (19.31%)	11 (7.59%)	18 (12.41%)	145 (100%)

The correlation between **pRIFLE Versus KDIGO based on Serum creatinine i**n diagnosing the AKI showed the **BEST AGREEMENT in stage III**

Out of 21 Stage 1 patients under pRIFLE, 14 agreed with KDIGO.

Out of 20 Stage 2 patients under pRIFLE, 6 agreed with KDIGO.

Out of 24 Stage 3 patients under pRIFLE, 16 agreed with KDIGO.

TABLE 29

Agreement between AKIN and KDIGO based on Serum Creatinine					
Serum Creatinine KDIGO	Serum Creatinine AKIN				
	Nil	Stage 1	Stage 2	Stage 3	Total
Nil	86 (61.43%)	05(3.57%)	1(0.71%)	00(0)	92(65.71%)
Stage 1	00(0)	22(15.71)	1(0.71%)	00(0)	23(16.43%)
Stage 2	00(0)	02(1.43%)	6(4.29%)	03(2.14%)	11(7.86%)
Stage 3	00(0)	00(0)	00(0%)	14(10%)	14(10%)
Total	86(61.43%)	29(20.71%)	09(5.71%)	17(12.14%)	140(100%)

Stage I of AKIN correlated well with Stage I of KDIGO based on serum creatinine

Stage III of AKIN correlated well with Stage III of KDIGO based on serum creatinine

TABLE 30

	Agreement between p-RIFLE and AKIN based on urine output (ml/kg/hr)				
	AKIN				
Urine output pRIFLE	**NIL**	**Stage 1**	**Stage 2**	**Stage 3**	**Total**
NIL	**126 (86.9%)**	**0**	**01 (0.69%)**	**0**	**127 (87.59%)**
Stage 1	**01 (0.69%)**	**01 (0.69%)**	**02 (1,38%)**	**01 (0.69%)**	**05 (3.45%)**
Stage 2	**0**	**0**	**05 (3.45%)**	**0**	**05 (3.45%)**
Stage 3	**0**	**0**	**02 (1.38%)**	**06 (4.14%)**	**08 (5.52%)**
Total	**127 (87.59%)**	**01 (0.69%)**	**10 (6.90%)**	**07 (4.83%)**	**145 (100%)**

In diagnosing AKI based on urine output, p-RIFLE and AKIN agreed with each other in **Stage 2 and 3.**

TABLE 31

Agreement between p-RIFLE and KDIGO based on urine output (ml/kg/hr)					
Urine p-RIFLE	**Urine KDIGO**				
	NIL	**Stage 1**	**Stage 2**	**Stage 3**	**Total**
NIL	**125 (86.21%)**	**02 (1.38%)**	**0**	**0**	**127 (87.59%)**
Stage 1	**01 (0.69%)**	**01 (0.69%)**	**03 (2.07%)**	**0**	**05 (3.45%)**
Stage 2	**0**	**0**	**05 (3.45%)**	**00**	**05 (3.45%)**
Stage 3	**0**	**0**	**02 (1.38%)**	**06 (4.14%)**	**08 (5.52%)**
Total	**126 (86.90%)**	**03 (2.07%)**	**10 (6.90%)**	**06 (4.14%)**	**145 (100%)**

Based on urine output, **p-RIFLE** and **KDIGO** agreed with each other **in Stage 2 and 3.**

TABLE 32

Agreement between AKIN and KDIGO based on urine output (ml/kg/hr)					
Urine AKIN	**Urine KDIGO**				
	NIL	**Stage 1**	**Stage 2**	**Stage 3**	**Total**
NIL	**125 (86.21%)**	**02 (1.38%)**	**0**	**0**	**127 (87.59%)**
Stage 1	**0**	**01 (0.69%)**	**0**	**0**	**01 (0.69%)**
Stage 2	**01 (0.69%)**	**0**	**09 (6.21%)**	**0**	**10 (6.90%)**
Stage 3	**0**	**0**	**01 (0.69%)**	**06 (4.14%)**	**07 (4.83%)**
Total	**126 (86.90%)**	**03 (2.07%)**	**10 (4.14%)**	**06 (4.14%)**	**145 (100%)**

In diagnosing AKI using **urine output <u>All the stages</u> correlate well with each other.**

AREA UNDER THE CURVES FOR pRIFLE, AKIN AND KDIGO BASED ON SERUM CREATININE

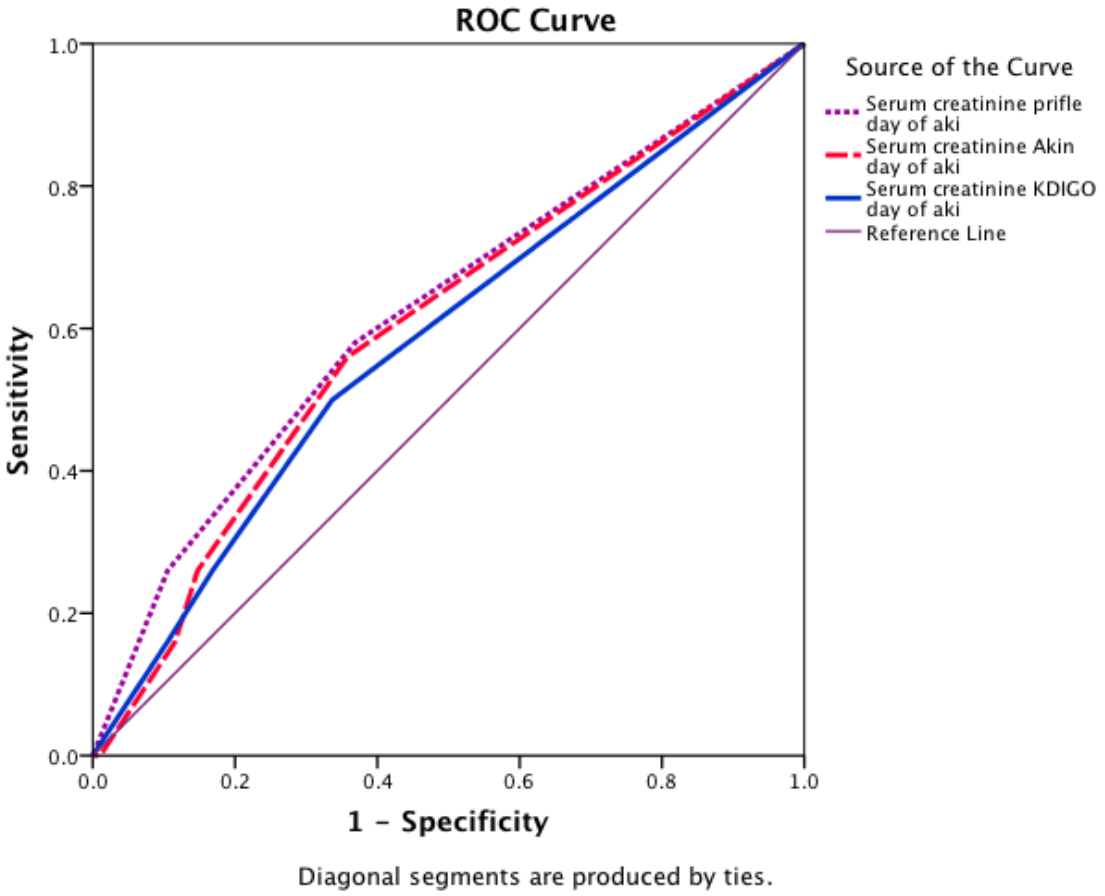

FIGURE 22

The predictive ability of p-RIFLE, AKIN and KDIGO (based on serum Creatinine) for in hospital mortality was compared.

Of these, none showed significant difference.Amongst these, p-RIFLE was most sensitive (58 %) but KDIGO was the most specific (67%) in predicting mortality in AKI children

.

PREDICTION OF MORTALITY USING SERUM CREATININE.

TABLE 33

Predictive Factor	Stage	Sensitivity	Specificity
pRIFLE	Stage 3 vs Stage 1	.45	.48
	Stage 2 Vs Stage 1	.44	.48
	Stage 3 Vs Stage 1&2	.24	.97

Predictive Factor	Stage	Sensitivity	Specificity
AKIN	Stage 3 vs Stage 1	0.36	0.36
	Stage 2 Vs Stage 1	0.30	0.83
	Stage 3 Vs Stage 1&2	0.16	0.94

Predictive factor	Stage	Sensitivity	Specificity
KDIGO	Stage 3 vs Stage 1	0.36	0.38
	Stage 2 Vs Stage 1	0.33	0.72
	Stage 3 Vs Stage 1&2	0.14	0.90

By all criteria, stage 3 AKI had the best specificity in predicting mortality in AKI

AUC FOR pRIFLE, AKIN AND KDIGO CLASSIFICATION

(BASED ON URINE OUTPUT)

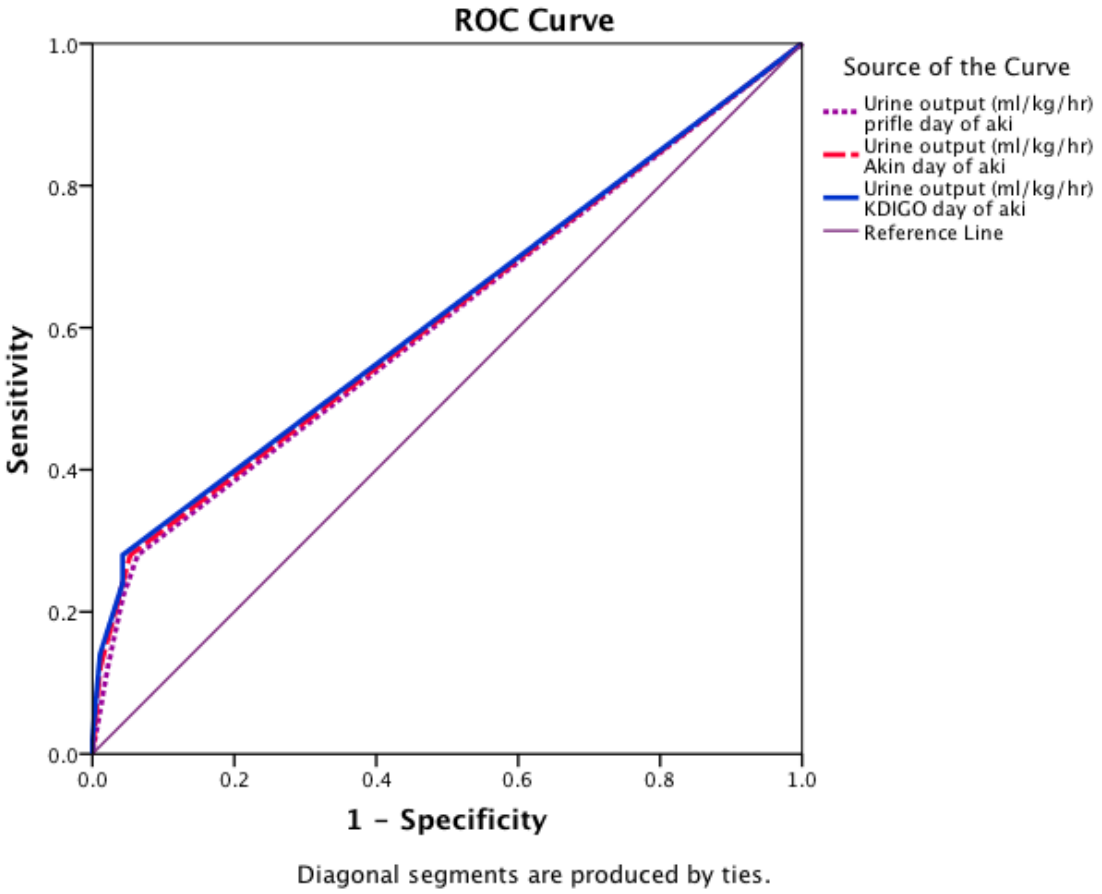

Figure 23

pRIFLE, AKIN and KDIGO based on urine output were not useful in predicting the mortality.

ASSOCIATION OF RENAL INDICES PREDICTING THE MORTALITY IN AKI

TABLE 34

Definition	Stage	Odds Ratio 95% CI	p-value
p-RIFLE	Risk	2.7(1.07-7.37)	0.048
	Injury	2 (0.72-5.59)	0.186
	Failure	3 (1.16-7.73)	0.023
AKIN	I	2.049(0.88-4.76)	0.098
	II	4.16(1.07-16.14)	0.039
	III	2.02(0.72-5.67)	0.183
KDIGO	I	1.89(0.78-4.56)	0.156
	II	2.52(0.74-8.56)	0.138
	III	1.76(0.6-5.15)	0.299

By pRIFLE, both stage 3 failure 3(1.16-7.73) and stage 1(Risk) 2.7(1.07-7.3) were good predictors of mortality..

By AKIN, Stage 2 (4.16 (1.07-16.14) was a good predictor of mortality(p-value=f 0.039)

By KDIGO none of stages were able to be predictive of mortality (p=> 0.05)

FOLLOW UP CREATININE

TABLE 35

Serum creatinine was followed up in 21 children

S.no	Follow up day	No of children
1	2-7	4
2	8-14	3
3	15-22	3
4	23-30	7
5	31-60	4

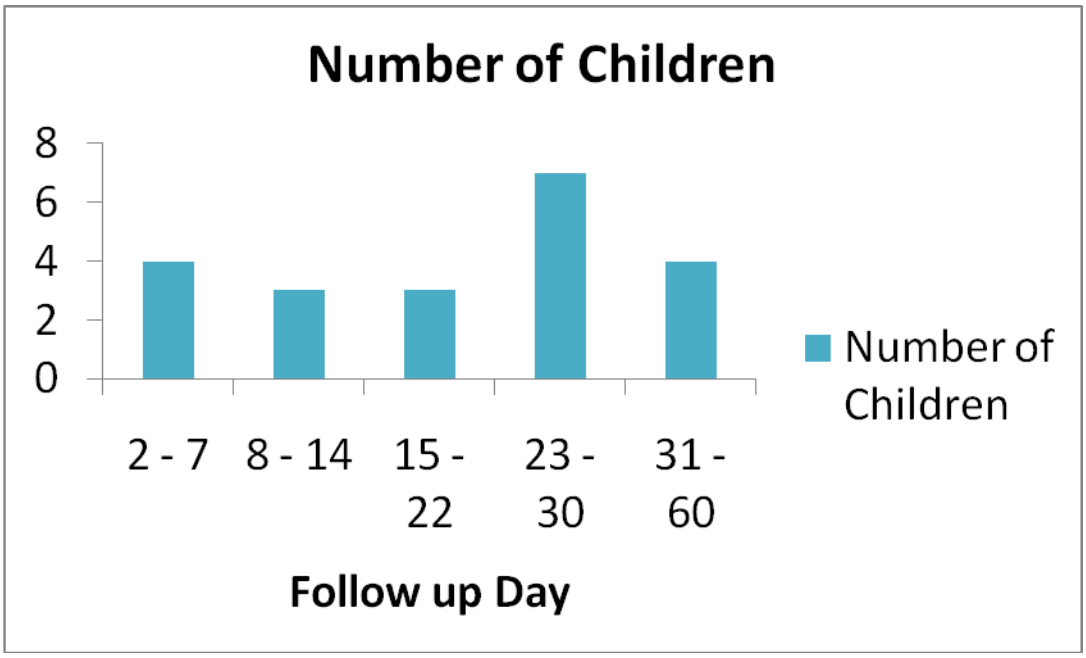

FIGURE 24

Out of the 48 children with AKI, 21 of them were followed up after discharge from2-60 days. .

Creatinine values ranged from 0.1- 2.89mg/dl.

At 4 weeks, two children had persistently elevated serum creatinine and were at risk of AKID

2/21 (4.16%)

DISCUSSION

This study was conducted under the Department of Paediatric Nephrology in Christian Medical College Hospital at Paediatric Intensive Care Unit .The aim of our study was to determine the incidence of AKI in critically ill children (0-15 Years). The three recent definitions used to diagnose AKI- namely pRIFLE, AKIN and KDIGO were applied in all patients and their ability to accurately diagnose AKI was compared. Their ability to predict the risk factors associated with AKI, length of hospital stay and outcome of AKI were also studied. The study was initiated after obtaining approval from Institutional Research Board and Ethics committee.

Acute Kidney Injury is a common complication associated with critical illness in children which either is a cause of hospitalization or a complication of illness in severely ill children admitted in an Intensive care unit. It is prevalent in both developing and developed countries causing increased morbidity and mortality. Prevention by early recognition and intervention at different levels (individual, community and hospital) may help to improve outcome. The importance of serial creatinine measurements and careful monitoring of the urine output particularly in the high risk groups needs to be recognized. The newer definitions define early AKI as a small rise in creatinine or a drop in urine output – if treated early, acute kidney disease may be prevented, along with the long term consequence of chronic kidney disease. A global strategy to decrease the burden of AKI needs to be developed.(23).

During the study period there were a total of 205 consecutive admissions to PICU. Of these 145 children who fulfilled the inclusion criteria and had none of the exclusion criteria were enrolled. Of the total, 60 were excluded. A total of 48 children were diagnosed with AKI. The data collected was statistically analysed and inferences were drawn

DEMOGRAPHIC CHARACTERISTICS

Of the study population of 145 children majority were between 0-2 years (37.2%), followed by 10-15 years (23.4%). The remaining were between 2-5 years (20.6%) and 5-10 years (18.6%).The median age of population studied was 3.4 years. Of this group 63% were boys and 37% were girls with male to female ratio of 1.7:1.0 (Table 1)

Amongst the 145 children,48 were diagnosed to have AKI thus showing an incidence of 33.1%. The global incidence of AKI among the critically ill children in PICU has been shown to be 33.7% (95% CI,26.9-41.3) by Li PKT, Burdmann etal(23)- which is identical to our findings.

DIAGNOSIS

The children who were admitted in PICU during the study period were grouped according to their presenting diagnosis. The most common diagnosis was infections, of which Sepsis was the predominant cause (23.6%) ,followed by neurological causes (20.0%), hematological causes (13.10),respiratory, cardiac and metabolic with 10.3%, 9.65%, 6.89% respectively. Of the remaining, dengue (20%), pneumonia (16.6%) and HLH (13.3%) were also common. This data is representative of morbidity at a particular period, during a specific time of the year- there may be some variations with season changes and also on a year to year basis. The median length of stay for the entire study population in PICU was 5 days with interquartile range (IQR) of 3 to 9 days.

RISK FACTORS

There are several risk factors which contribute to the morbidity and outcome. Some of these may be based on the initial presenting symptoms and signs- while others may be due to interventions that need to be instituted to overcome these complications. The presentation of shock (52.4%) and the need to give multiple fluid boluses was followed by the use of inotropes (in 57.2%) in our study and mechanical ventilation was required in 66,2% of our patients. Blood support was required in as many as 66.8% ; while nephrotoxic medications were administered in only few children in (2.06%). All these may be considered as risk factors for the development of AKI

Among the total study population, AKI was diagnosed in 48 children based on rise in serum creatinine or fall in urine output according to the definitions proposed by Acute Dialysis Quality Initiative in 2002(28). The children were divided in to two groups AKI and Non AKI The demography and clinical characteristics of these two groups were compared.

INCIDENCE OF AKI:

The overall incidence of AKI in this study population was 33.1% (48/145) based on serum creatinine and.24.1% based on urine output. Incidence of AKI according to serum creatinine measurement was higher when compared to urine output. In a prospective study by Krishnamoorthy et al (3) in southern population of India, the incidence was 25.1% while Mehta et al (52) reported a much higher incidence of 45.1%. In another study by Xiong , Tang X et al reported the incidence of AKI to be 3.9/1000 admissions.(11) Keenswijk in his retrospective cohort study reported the incidence to be much higher at 5.9/1000 children(13). Rovetto et al studied children between an age group of 30 days to 18 years over a period of seven months. He reported the AKI incidence to be 16 times higher in PICU patients compared to ward

patients (32).The higher incidence in some of the previous studies is not clear, but may be due to different disease characteristics which may vary from region to region..

DEMOGRAPHIC CHARACTERISTICS

There were a total of 48 children who were diagnosed with AKI. These children were evaluated further for their disease characteristics, clinical course and outcome. Majority of these children were in the age group of 0-2years (37.2%) followed by the age group 10-15 years (23.4%). A study by Al-jaboor reported the median age of children with AKI in a PICU admitting children between 1-14 years to be 5.4 years. (53). In an Indian study by Krishnamurthy et al the median age of patients with AKI was 21 months (range 1-144 months); there were 53.7% boys (56) In the Agarwal study (2004) also ,46% (25/54) of the children were in the age group of infants, 19 (35%) belonged to the 1- 5 year group and 10 (19%) were 6 years and above

In our study, amongst children with AKI, males outnumbered females ((56% vs 44%). In a similar study on 92 children, though retrospective by Agarwal I et al (2004) males again predominated 54/38 -70%)(54).K Keenswijk also reported more male children to have AKI (13).

The incidence of AKI in the present study were assessed by two parameters namely serum creatinine and urine output, and all three Definition criteria were applied. The incidence according to pRIFLE, AKIN and KDIGO was 33.1% based on serum creatinine in all. In a prospective Multicentric study in 30 ICU settings of 28 tertiary centers performed by Jiang. Li et al (39) incidence of AKI was found to be 46.9%,38.4% and 5%. In another retrospective

study by Sutherland et al with a huge study population of 14,795 study population over a period of 5 years (22) AKI was reported in 51.1%,37.3%,40.3% respectively.

In the present study, the inter-stage incidence of AKI according to p-RIFLE with Stages I II and III- were 48%,12% and 39.5%,respectively. By AKIN Stages I, II and III were 48%, 10% and 41.6% respectively. When the KDIGO definitions were applied, the number of children diagnosed in the various stages were 50%, (stage I) 8% (Stage II), and 41.6% (Stage III) respectively. Thus we can see that all the three definitions reported a similar incidence of AKI in spite of having some differences in their definitions. In a similar prospective study by Jiang Li et al who also compared the 3 criteria for diagnosing AKI, the same inter-stage incidences were noted. By pRIFLE, AKI was diagnosed according to Stages I, II and III and were 20.8%,12.4% and 13.8% respectively. Using the AKIN criteria, the number of children in Stage I were 19%, stage II were 6.6% and stage III were 13.8%. When the KDIGO definitions were used, the following were obtained- stage I (23.1%), Stage II (11.8%) and Stage III 16% .(39). While the results were similar and comparable, it appeared that stage II criteria was identified almost equally by pRIFLE and KDIGO, but not by AKIN. Sutherland reported that pRIFLE AKI in Stages I- II- III- to be 26.9%,13.4% and 10.8% while in AKIN reported Stage I (19.4%), Stage II (11.2%)and stage III 6.7% respectively. KDIGO identified AKI in Stages I, II, III- in the following manner- 18.2%,10.4% and 11.7% respectively.(22) In his study, all the stages were almost similar, except stage I by KDIGO criteria, where the identification was much lower compared to the other groups. The overall incidence of AKI varied between these studies, but the criteria for diagnosis were not vastly different. In our study, as some of the others, majority of the children were diagnosed in either stage I or III, with the least number being diagnosed in stage III (based on serum creatinine).

These criteria were also applied to diagnose AKI based on the urine output to define the different stages. By this method also, all the three stages showed no difference, though the overall incidence of AKI, in the same population of patients, was much lower than the creatinine clearance criteria. The reason for this may be that most of the most of the children had Non oliguric renal failure, though this is not a common finding in critically ill children.

S.No.	Study	Place/Year	pRIFLE %	AKIN %	KDIGO %
1	Sutherland etal(n=14975)	USA/2006-10	17.03	12.43	13.43
2	Kavaz etal (n=189)	2012	35.9	33.3	-
3	Jiang Li etal (n=3107)	(China)2012	15.6	13.13	16.97
4	Zeng et al (n=31970)	2014	16.1	16.6	18.3
5	Luo etal (n=438)	2017	46.9	38.4	51
6	Present study(145)	India/2017	33.17	33.2	33.2

As evident from the above comparison between our data and other studies, our study detected more children with AKI whichever definition was used.

ETIOPATHOGENESIS

In the present study the various clinical diagnosis contributing to AKI were infection (29.1%), neurological illness (18.75%), hematological diseases (12.5%) and respiratory illnesses (10.4%). Diabetic ketoacidosis as a cause of AKI was seen in (8.3%), and others were (25.3%). Among these, the most common cause of AKI was Sepsis. Amongst the Non AKI children, the most common diagnoses were similar-infections (20.6%), followed by neurological (20%), hematological (13%), respiratory (10.2%) cardiac (9.6%), and metabolic (6.8%) respectively. A retrospective study was conducted in our institution by Agarwal I et al (2004) to assess the clinical profile of children admitted with acute renal failure and to identify factors associated with poor outcome. The leading precipitating causes for renal failure were acute gastro-enteritis (85%), underlying renal pathology (43%), proven sepsis (22%) and suspected sepsis (22%). The main presenting complaints were diarrhoea (86%),oliguria (72%), rapid respiration (37%), oedema (37%), vomiting (19%) and seizures (13%).(18) . In our current study children with preexisting renal disease were excluded. Acute gastroenteritis was a major cause of AKI in the previous study, but in the present setting, with education and wider distribution and use of ORS, it no longer remains as the predominant cause of AKI. However, sepsis still remains as one of the major causes of admission to PICU with subsequent AKI.

In a prospective study of 215 children diagnosed with AKI in PICU over a period of 10 months by Krishnamurthy et al the common etiologies reported were infections(55.4%) acute Glomerulo nephritis (16.9%) and tropical febrile illnesses 15.6%(3) Amongst them sepsis constituted (26.5%), followed by pneumonia (26.1%) and Meningoencephalitis (23.5%) which were similar to our study(2). Amira Peco-Antic described that AKI results from various causes

like sepsis , nephrotoxins than from intrinsic renal diseases like glomerulonephritis (19) In our study we did not include pre existing renal diseases- this may account for some of the differences in our results. A study done by Sadeghi-Bojds found that the most common PICU admission diagnosis in AKI were neurological (28.05%), heart disease (17.18%) and respiratory diseases (10.23%) (20) In our study, while sepsis accounted for 29.1%, the other illness like neurological (18.75%,) and respiratory (12.5%) and hematological (10.4%) were somewhat similar.

RISK FACTORS FOR AKI

In this study the risk factors for the occurrence of AKI were studied. Shock (60.4%), inotropes use (72.9%), need for mechanical ventilation (70.8%) were the most common parameters noted. The presence of shock significantly contributed to the development of AKI. Similar to our results, Gupta et al, in a prospective observational study of 230 patients with AKI reported the risk factors to be shock (60.86%) and mechanical ventilation (34.7%) (4). Children requiring ventilation was almost double that reported in this study.

In another study by Mehta et al again sepsis and mechanical ventilation were reported to be independent risk factors for AKI (28). Rustagi et al also reported shock to be a significant risk factor contributing to AKI. In a univariate analysis by Shweta Naik et al on 103 patients, shock (23.8%) and mechanical ventilation(21.4%) again were significant risk factors for development of AKI (55) .

Gist K M et al in his study stated Milrinone, an inotropic drug chiefly excreted in an unchanged form is known to worsen renal function in children with preexisting AKI(16). Nephrotoxic drugs are also important risk factors for AKI in children, and were responsible for 16% of AKI

according to Patzer L(15). In our study, however, nephrotoxic drugs were used in 2.06 %- of these also only 4.1% developed AKI. Careful dosing of these drugs (renal adjustment) as well close monitoring of renal function in these children may explain the reason for the low incidence.

BASAL CREATININE:

Baseline creatinine is defined as the lowest serum creatinine value in the previous 3 months. Estimating of the baseline glomerular filtration rate (GFR) is done using the original Schwartz equation.(29) and serum creatinine. In our study we used serum creatinine to calculate renal function, using the modified Schwartz formula. The baseline creatinine which is required to diagnose AKI was calculated from the lowest creatinine available in the last three months. For those children who did not have the value serum creatinine value was taken from the age appropriate values.

Diagnostic criteria:

In our study Serum Creatinine and urine output were used to diagnose AKI according to the ADQI guidelines (2002) (56) The study was designed on the model of another conducted by Xuying Luo who categorized patients based on serum creatinine, urine output or both however in the final analysisonly serum creatinine has been reported in their study. (39) Scott Sutherland designed his study **only using Serum creatinine** (22). Cabral et al used serum creatinine and urine output employing pRIFLE to diagnose AKI but did not use the other criteria.(43), Kellum et al in their study used the Serum Creatinine value (within 48 hour)ineand urine output over the same period to diagnose AKI. All the above studies thus supported the use of serum creatinine in

the diagnosis and staging of AKI. Our study was the only study to do a prospective study on children with AKI using both the Creatinine and the urine output for defining AKI

pRIFLE CRITERIA

In our study pRIFLE criteria using Serum Creatinine and urine output had more sensitivity and also had better predictability in diagnosing AKI (58% sensitivity and 64% specificity) pRIFLE was also utilized by several other studies in an attempt to validate it as a tool for diagnosing AKI. Al-jboor et al reported that pRIFLE was better for early detection of AKI and thereby was helpful in reducing the morbidity and mortality(53). Similarly a study by Plotz Bouma et al found that pRIFLE identified patients at risk for AKI far earlier and were thus able to treat better.(35). Rovetto et al who used the pRIFLE also reported it to be a useful tool for early diagnosis, classification and prognosis of AKI(32). In another study by Yong K Dogra et al pRIFLE served as a good prognostic tool in assessing the morbidity and mortality in children with AKI(34). Similar to our study Kavaz et al found pRIFLE to be more sensitive in detecting AKI(36)

AKIN CRITERIA

The AKIN criteria were also applied in our study population and was found to be useful in the diagnosis of AKI in stage I and Stage III. The number of children detected to have Stage II was less compared to other criteria. In a south Indian study by Srinivasa et al higher incidence of AKI was noted by AKIN in comparison to pRIFLE(28). After completing a similar study, Prasad etal reported that AKIN criterion's utility is limited because it utilizes rise in serum creatinine within a short time frame of 48 hours only(10). In another study by Sutherland et al

also proved the inability of AKIN criteria to identify 427 patients with AKI which were however diagnosed by pRIFLE and KDIGO (40) in the same study group.

KDIGO DEFINITION

In our study, using serum creatinine KDIGO was able to diagnose more number of cases of AKI in stage I and stage III. When urine output criteria by KDIGO was applied, it was shown to be more sensitive (79%) and also showed a better predictive value. A study done by Luo et al stated that a higher number of children were diagnosed to have AKI using the KDIGO criteria. It was also a better predictor of in-hospital mortality.(39), Ostermann et al defined AKI based on the rise in serum creatinine or / and fall in urine output according to KDIGO(37) . Selewski et al found a higher prevalence of AKI in critically ill children using KDIGO, and reported that it defined clinically relevant AKI in children(57)

From our study and the other studies quoted pRIFLE is more sensitive in the early detection of AKI when compared to AKIN and KDIGO because it has detected more number of cases and has better predictive ability with regard to mortality. Based on urine output the number of cases diagnosed as AKI were far less in number than that by Serum creatinine. There were no other studies available for comparison as all studies were retrospective and there were none where Urine output was taken as a criteria. Studies by Xuying Luo et al (39) and Sutherland et al (40) and the present study were the studies which have used the three criteria .

LENGTH OF HOSPITAL STAY

In the present study the median length of stay (LOS) in PICU for children with AKI was 7 days (IQR of 3.52-12), according to all the three criteria p RIFLE, AKIN and KDIGO. In stage 1 LOS was longer when compared to stage 3 which can be explained by more critical illness in those with stage 3 disease and therefore shorter hospital stay in view of poor outcome. However there was no significant association between the length of stay and mortality according to the three criteria in our study.

In a study by Basu etal the mortality and length of hospital stay is increased to four fold in children diagnosed to have AKI.(21).A similar study by Alkandari et al also found that the diagnosis of AKI in critically ill children resulted in longer length of hospital stay (44). Studies conducted by Kavaz etal ,Chang J-W etal, Volpon etal and Shalaby etal all found similar results of longer length of stay(36),(45),(46),(42) in critically ill children admitted in an Intensive care.

Outcome

In the present study out of 48 children diagnosed with **AKI 66.6% completely recovered and were discharged, 10.4% showed partial improvement, 18.8% developed AKD and 4.2% were dialysis dependen**t. The mortality in critically ill children was more in those diagnosed with AKI when compared to Non- AKI. The renal outcome using p RIFLE showed 30 (62.5%) children improved and discharged, 5 (10.4%) showed partial improvement, 9 (18.74%) developed AKD and 2 (4.2%) were dialysis dependent. Using AKIN 30 children (63.81%) showed improvement, 4 (8. 5%) showed partial improvement, 9 (19.1%) developed AKD and 2(4%) became dialysis dependent. Using KDIGO the renal outcome showed 30 (63%) were discharged because of improvement, 4 (8.5%) partially improved, 9 (19.1%) developed AKD

and 2 (4.4%) were dialysis dependent. The ability to predict the outcome in all the three stages using the definitions were similar.

In his study Keenwijk etal stated that children who presented initially with failure required RRT(13). Rustagi etal stated that higher mortality was associated with AKI diagnosed using pRIFLE(58), Shalaby etal found pRIFLE criterion predicted higher mortality in stage III (42), Volpon etal showed using pRIFLE criteria AKI was associated with better prediction of morbidity and mortality(46). In another study by Rashid Alobaidi etal new strategies were recommended to reduce the poor outcome of AKI using clinical risk identification, early detection of injury instituting early antimicrobial therapy and surveillance of long term sequelae in survivors.(14). In a study by Otaibi etal, large proportion of patients who were admitted to PICU with AKI died during first 2 years or developed long term complications(59). Murugan etal in their study showed that the survivors of AKI develop long term complications like Chronic Kidney Disease and End Stage Renal Disease (60). In a recent study, Anil Vasudevan et al (2017) showed that infants and children become dependent on renal replacement therapy. Peritoneal dialysis provides adequate clearance and corrects metabolic irregularities.(51). In their study, Touza Pol etal found out that critically ill children diagnosed to have AKI had an increased mortality and morbidity rate. In a study by Soler etal AKI diagnosed by pRIFLE and fluid overload greater than or equal to 10% led to the increased morbidity and mortality. They reported that the use of pRIFLE scoring and close monitoring of fluid overload helps to prevent and treat AKI in children(61). In a study by Schneider etal it was shown that AKI on admission or during PICU stay, diagnosed by pRIFLE using Serum Creatinine was associated with increased PICU mortality and length of hospital stay(62). A study by Gomez Polo etal also revealed the presence of AKI in critically ill children to be associated with higher morbidity and

mortality proportional to the amount of renal injury (63). In a study by Gupta etal, presence of AKI in critically ill children was reported to be associated with higher mortality. They suggested effective ways to detect early and reduce the mortality due to AKI(64).

RENAL REPLACEMENT THERAPY

Out of total 48 children with AKI, 14 (29.1%) required dialysis. In a study by Sanchez Pinto etal they concluded that the requirement of RRT was not related to the etiology or age of the patient (48). Ten children (20.8%) underwent peritoneal dialysis while 4(8.3%) required Hemodialysis In. a similar study by Krishnamurthy etal reported that 28.7% AKI patients required RRT(47). A Study by Vasudevan et al stated that peritoneal dialysis is the modality choice of RRT in AKI as it is simple, safe and inexpensive procedure (51). Though RRT serves as the better modality of treatment, the need for RRT itself is a risk factor and is predictive of increased mortality in children with AKI. This was also shown by studies done by Keenswijk etal and Shalaby etal wherein they found that AKI children who required RRT during the management had increased mortality.(13)(42).The **mortality for those on RRT in our study was also high as 71.2% children** succumbed to their illness inspite of all interventions.

A study by Ciccia and Devarajan stated that hemodialysis has its own difficulties as access remains a great challenge, as well as exposure to blood products and risk of fluid overload or losses in small children (30) . These factors could also pose a risk to the child and increase mortality.

The PIMS (Paediatric Index Mortality of Scoring) was used to estimate the mortality of children diagnosed with AKI. However in our study we were unable to apply the score in all patients,

hence we were able to predict mortality for only some of the patients. The main reason for this was the difficulty in availability of complete data in several of the patients in our study population. Alkandari et al who carried out a retrospective study, reported that the Paediatric Index of Mortality underestimated mortality in children with AKI

A prospective study was carried out by Jeyanthi Gandhi etal using the PIMS score to predict the outcome of critically ill children in PICU. They also found that PIMS score differentiated the survivors and non survivors amongst these critically ill children well(65). In another study, Cabral etal stated that the median Pediatric Index of Mortality 2 score predicted a mortality rate of 9% in non-acute kidney injury patients versus a mortality rate of 16% in acute kidney injury patients ($p = 0.006$)(43)

INTERSTAGING AGREEMENT

In our study AKI was diagnosed using all definitions pRIFLE, AKIN, and KDIGO. They showed comparable associations with similar outcomes according to the severity of staging. The agreement between AKIN versus p-RIFLE was good, but the agreement between pRIFLE and KDIGO was the best. The agreement between AKIN and KDIGO also showed best agreement in stage 1 and stage 3. Based on urine output all the classifications had good agreement with each other.

In their by study, Xuying et al showed excellent association with adverse outcome and severity of AKI**(39)**. In an another study by Scott etal good associations among the three classifications in diagnosing AKI**(22)** was also reported.

PREDICTIVE ABILITY OF MORTALITY:

Amongst the 48 children with AKI using p RIFLE staging, **the odds of mortality was 2.71 and 3,** in patients with risk and failure respectively (p=<0.05). Using AKIN staging, the odds of mortality was 2 with a p-Value of 0.039. By KDIGO staging, none of the stages were able to significantly predict mortality. The study by Jiang **(66)** was able to highly significant association with mortality in all stages of AKI and by all definitions,

On comparing the predictive ability of p-RIFLE, AKIN and KDIGO based on serum Creatinine to predict mortality, none of them could show any significant association. However, amongst them, p-RIFLE was more sensitive and a better predictor of mortality (58% sensitivity).

ASSOCIATION OF RENAL INDICES

Present Study				Xuying Luo et al	
Definition	Stage	Odds Ratio 95% CI	p-value	Odds Ratio (95% CI)	P value
p-RIFLE	**Risk**	**2.7(1.07-7.37)**	**0.048**	1.96(1.46-2.64)	<0.001
	Injury	2 (0.72-5.59)	0.186	3.48(2.55-4.75)	<0.001
	Failure	**3 (1.16-7.73)**	**0.023**	6.95(5.19-9.30)	<0.001
AKIN	I	2.049(0.88-4.76)	0.098	2.62(1.99-3.45)	<0.001
	II	**4.16(1.07-16.14)**	**0.039**	4.63(3.22-6.65)	<0.001
	III	2.02(0.72-5.67)	0.183	7.75(5.82-10.32)	<0.001

On comparing the predictive ability of pRIFLE AKINand KDIGO basedon serum creatinine to predict mortality, none of them could show any significant association.However pRIFLE appeared to be the most sensitive

When the predictive ability of p-RIFLE, AKIN and KDIGO were compared - based on urine output- again neither of them could predict hospital mortality. Of these however, KDIGO appeared to be the most sensitive and predictor of mortality.

Xuying Luo etal reported that irrespective of the definition used, the in- hospital mortality was significant when AKI was diagnosed. They however concluded that mortality was higher in patients diagnosed with AKI using KDIGO rather than p RIFLE(39)

SUMMARY

SUMMARY

This was a prospective study done to assess the correlation between different criteria in diagnosing AKI and also find the incidence, length of stay, association of risk factors , outcome of illness in critically ill children with AKI admitted in Paediatric Intensive Care Unit.

1. Out of 145, Forty eight children with AKI were between the age group 0-15 years were studied .
2. Males were predominant, with Male : Females (1.3 :1)
3. The most common etiological diagnoses in the study population were **Sepsis(23.3%)** followed by Neurological illnesses(20%),Haematotological (13.1%) followed by, respiratory (10.3%) cardiac (9.6%) and metabolic (6.8%) respectively
4. Using the different criteria based on serum creatinine , and urine output the incidence of AKI was 33.1%. and 24.1% .
5. The risk factors associated with AKI were blood components to correct coagulopathy and use of respiratory nephrotoxic drugs while the interventions were use of ionotropes and mechanical ventilation. There was a significant association between AKI and the occurrence of shock and the need for mechanical ventilation.
6. Of the interventions, 72.9% were treated with inotropes (p value <0.01), 81.3% required mechanical ventilation.Blood support were used in 66.8% where as Nephrotoxic medications were used only in 2.06%
7. The occurrence of shock, p value(<.05) use of inotropic support(p value=0.<01 , and Ventilation had a highly significant (p= <0.001) association with the risk of developing AKI.
8. All patients were subjected to standard investigations and treatment. Of the total, (48) 14 received renal Replacement treatment.(29.17%), 11 peritoneal dialysis (71.4%) and 3 hemodialysis(28.5%).Mortality amongst those on RRT was 71%

9. Overall outcome for AKI included complete recovery in 28(58.3%), 14(29.1%) deaths, and 6 (12.5%) discharged against medical advice.

10. Renal outcome: 32(66.6%) children improved completely, 5(10.4%) showed partial improvement ,9 (18.8%) developed AKD and 2 (4.2%) were dialysis dependent. The renal outcome was significantly worse in children with AKI than Non AKI ($p<0.001$)

11. The median length of stay in children with AKI was 7 days. There was no significant difference between the length of stay of children and the mortality by any criteria.

12. All the three definitions were in agreement with each other with regard to the incidence and diagnosis of AKI

13. Using p RIFLE criteria more children with AKI were detected. ($p<0.023$) value Using AKIN more children improved in stage I and had a higher mortality in stage III. KDIGO predicted good improvement in stage I. The predictability of mortality was similar with all three definitions.

14. There was no significant difference in the predictive ability of p-RIFLE, AKIN and KDIGO (based on serum Creatinine) for in hospital mortality. However, p-RIFLE was the most sensitive and was the best predictor of mortality.

15. The correlation between pRIFLE, AKIN and KDIGO in diagnosing AKI based on serum creatinine showed good agreement

16. The correlation between p RIFLE, AKIN and KDIGO in diagnosing AKI based on urine output showed good agreement.

17. Children who were discharged on follow up with repeat creatinine, two children had established kidney disease out of twenty one .(4.16%)

CONCLUSION

CONCLUSION

Mortality with AKI inspite of improvement in treatment still remains a area of concern even in developed countries. Using the different definitions to stage AKI for early detection, which will help in early intervention and institution of appropriate treatment will be the key to improve the outcome.

1. The Incidence of AKI among critically ill children aged 0-15 years was 33.1% using all the 3 definitions.
2. The commonest cause of AKI was infections followed by neurological causes.
3. The Inter definition agreement between the three definitions for AKI was good
4. Acute renal injury was better diagnosed using creatinine criteria than urine output criteria.
5. Of the children with AKI 29% of children required Renal replacement therapy
6. Mortality in children with AKI was 29.1% and mortality in those on RRT was 71%.
7. pRIFLE was the best predictor of mortality amongst stabe 3 patients when compared to AKIN and KDIGO.
8. On follow up 21 out of 48 AKI children who were followed up 2 had established kidney disease.

LIMITATIONS

The Predictive ability of the three definitions used in this study would have been better if the duration of study and the sample size were higher.

RECOMMENDATIONS :

Though each definition has its advantages, all the three criteria are in agreement with each other. No single definition needs to be recommended as any of these criteria may be adopted in a PICU setting.

We recommend that all Intensivists strictly monitor critically ill children using these and of these definitions. This will facilitate early detection of AKI and will translate into earlier interventions and better outcome.

ABBREVIATIONS

AKI: Acute kidney injury

ADQI: Acute Dialysis Quality Initiative

AKIN: Acute Kidney Injury Network

AUC: Area under the curve

CI: Confidence Interval

ESKD: End-Stage Kidney Disease

GFR: Glomerular filtration rate

PICU: Paediatric Intensive Care Unit

IQR: Interquartile range

KDIGO: Kidney Disease: Improving Global Outcomes

OR: Odds Ratio

pRIFLE: Paediatric Risk, Injury, Failure

Loss of Kidney Function and End-stage Kidney Disease

ROC: Receiver Operating Characteristic

RRT: Renal Replacement Therapy

SCr: Serum Creatinine

bCr: basal Creatinine

PIMS:Paediatric Index of Mortality Scoring.

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ANNEXURE

ANNEXURE 1-CLINICAL PROFORMA

ANNEXURE 2-MASTER COPY

ANNEXURE 3-PATIENT INFORMATION SHEET

ANNEXURE 4-CONSENT FORM

ANNEXURE 5-IRB APPROVAL

Study of AKI in critically ill children using different Renal Indices

PROFORMA

Name- Hospital number -
Date-
Sex- Boy / Girl Age- yrs
Address-

Weight - kg Height- cm

Duration of disease before presentation to Hospital - days

Prior hospitalization – Yes / No- if Yes - days

History:

1. Fever	Yes	No
2. Number of days into illness	Yes	No
3. Rash	Yes	No
5. Bleeding manifestation	Yes	No
6. Ascites	Yes	No
7. Breathlessness	yes	No
8. Impairment in sensorium	Yes	No
9. Blood investigations done else where	Yes	No
10. Any nephrotoxic drugs given elsewhere	Yes	No
11.		
12. If yes, how many doses –		

	At admission	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9
TEMPERATURE										
HEMOGLOBIN										
PLEURAL EFFUSION ON CHEST XRAY										
HEPATOMEGALY										
ASCITES										
BLEEDING MANIFESTATION										
SHOCK										
INOTROPES										
BLOOD TRANSFUSION										

13. Shifted to PICU/HDU ☐ Yes ☐ No

14. on day _____ of admission

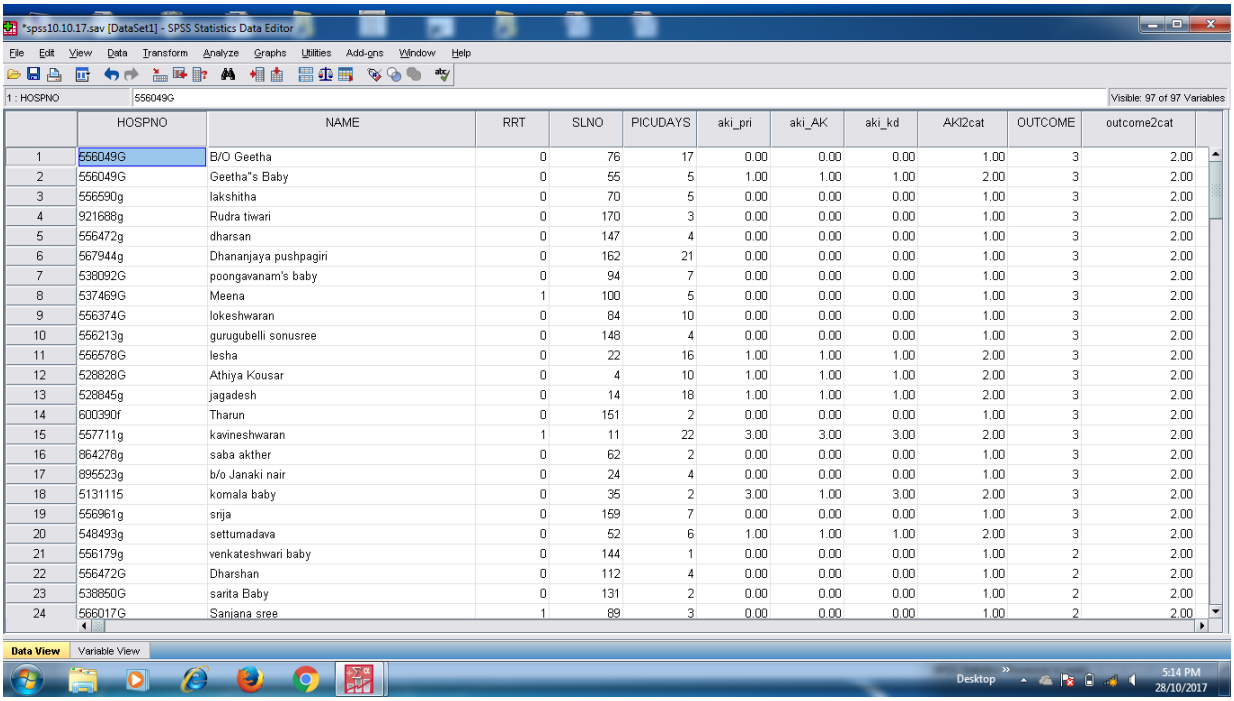
Serum Creatinine at admission- mg/dl

	Day 1	Day 2	Day 3	Day 4
Serum creatinine (mg/dl)				
Creatinine clearance(Schwartz)				
Urine output(ml/kg/hr)				
AKIN Stage Prifle Stage KDIGO Stage				

<u>Mechanical Ventilation</u>: ☐ ☐

If yes ☐ <72 hours ☐ >72
hours
Nephrology consultation: ☐ ☐
Renal replacement therapy: ☐ Yes ☐ No
Type of RRT: ☐ PD ☐ IHD ☐ SLEDS ☐
CVVHD
Number of days in PICU::
Outcome: Discharged/ Death / DAMA / RRT

MASTER COPY



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1 : HOSPNO 556049G Visible: 97 of 97 Variables

	HOSPNO	NAME	RRT	SLNO	PICUDAYS	aki_pri	aki_AK	aki_kd	AKI2cat	OUTCOME	outcome2cat
1	556049G	B/O Geetha	0	76	17	0.00	0.00	0.00	1.00	3	2.00
2	556049G	Geetha"s Baby	0	55	5	1.00	1.00	1.00	2.00	3	2.00
3	556590g	lakshitha	0	70	5	0.00	0.00	0.00	1.00	3	2.00
4	921688g	Rudra tiwari	0	170	3	0.00	0.00	0.00	1.00	3	2.00
5	556472g	dharsan	0	147	4	0.00	0.00	0.00	1.00	3	2.00
6	567944g	Dhananjaya pushpagiri	0	162	21	0.00	0.00	0.00	1.00	3	2.00
7	538092G	poongavanam's baby	0	94	7	0.00	0.00	0.00	1.00	3	2.00
8	537469G	Meena	1	100	5	0.00	0.00	0.00	1.00	3	2.00
9	556374G	lokeshwaran	0	84	10	0.00	0.00	0.00	1.00	3	2.00
10	556213g	gurugubelli sonusree	0	148	4	0.00	0.00	0.00	1.00	3	2.00
11	556578G	lesha	0	22	16	1.00	1.00	1.00	2.00	3	2.00
12	528828G	Athiya Kousar	0	4	10	1.00	1.00	1.00	2.00	3	2.00
13	528845g	jagadesh	0	14	18	1.00	1.00	1.00	2.00	3	2.00
14	600390f	Tharun	0	151	2	0.00	0.00	0.00	1.00	3	2.00
15	557711g	kavineshwaran	1	11	22	3.00	3.00	3.00	2.00	3	2.00
16	864278g	saba akther	0	62	2	0.00	0.00	0.00	1.00	3	2.00
17	895523g	b/o Janaki nair	0	24	4	0.00	0.00	0.00	1.00	3	2.00
18	5131115	komala baby	0	35	2	3.00	1.00	3.00	2.00	3	2.00
19	556961g	srija	0	159	7	0.00	0.00	0.00	1.00	3	2.00
20	548493g	settumadava	0	52	6	1.00	1.00	1.00	2.00	3	2.00
21	556179g	venkateshwari baby	0	144	1	0.00	0.00	0.00	1.00	2	2.00
22	556472G	Dharshan	0	112	4	0.00	0.00	0.00	1.00	2	2.00
23	538850G	sarita Baby	0	131	2	0.00	0.00	0.00	1.00	2	2.00
24	556017G	Sanjana sree	1	89	3	0.00	0.00	0.00	1.00	2	2.00

Data View Variable View

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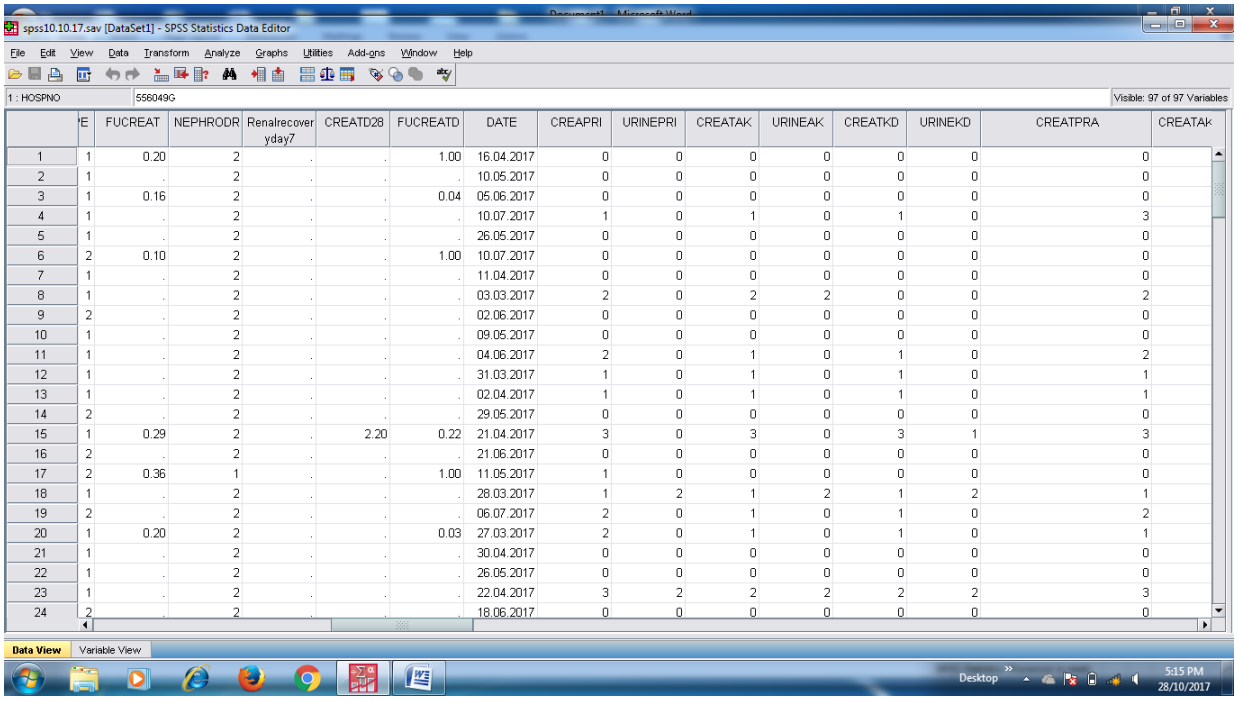

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1 : HOSPNO 556049G Visible: 97 of 97 Variables

	E	FUCREAT	NEPHRODR	Renalrecoveryday7	CREATD28	FUCREATD	DATE	CREAPRI	URINEPRI	CREATAK	URINEAK	CREATKD	URINEKD	CREATPRA	CREATAK
1	1	0.20	2	.	.	1.00	16.04.2017	0	0	0	0	0	0	0	
2	1	.	2	.	.	.	10.05.2017	0	0	0	0	0	0	0	
3	1	0.16	2	.	.	0.04	05.06.2017	0	0	0	0	0	0	0	
4	1	.	2	.	.	.	10.07.2017	1	0	1	0	1	0	3	
5	1	.	2	.	.	.	26.05.2017	0	0	0	0	0	0	0	
6	2	0.10	2	.	.	1.00	10.07.2017	0	0	0	0	0	0	0	
7	1	.	2	.	.	.	11.04.2017	0	0	0	0	0	0	0	
8	1	.	2	.	.	.	03.03.2017	2	0	2	2	0	0	2	
9	2	.	2	.	.	.	02.06.2017	0	0	0	0	0	0	0	
10	1	.	2	.	.	.	09.05.2017	0	0	0	0	0	0	0	
11	1	.	2	.	.	.	04.06.2017	2	0	1	0	1	0	2	
12	1	.	2	.	.	.	31.03.2017	1	0	1	0	1	0	1	
13	1	.	2	.	.	.	02.04.2017	1	0	1	0	1	0	1	
14	2	.	2	.	.	.	29.05.2017	0	0	0	0	0	0	0	
15	1	0.29	2	.	2.20	0.22	21.04.2017	3	0	3	0	3	1	3	
16	2	.	2	.	.	.	21.06.2017	0	0	0	0	0	0	0	
17	2	0.36	1	.	.	1.00	11.05.2017	1	0	0	0	0	0	0	
18	1	.	2	.	.	.	28.03.2017	1	2	1	2	1	2	1	
19	2	.	2	.	.	.	06.07.2017	2	0	1	0	1	0	2	
20	1	0.20	2	.	.	0.03	27.03.2017	2	0	1	0	1	0	1	
21	1	.	2	.	.	.	30.04.2017	0	0	0	0	0	0	0	
22	1	.	2	.	.	.	26.05.2017	0	0	0	0	0	0	0	
23	1	.	2	.	.	.	22.04.2017	3	2	2	2	2	2	3	
24	2	.	2	.	.	.	18.06.2017	0	0	0	0	0	0	0	

Data View Variable View

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PATIENT INFORMATION SHEET

Study of Acute Kidney Injury in Sick Children using different Renal Indices

Information sheet for the Parents/Guardian

Acute kidney injury is a common illness seen in sick children admitted in paediatric intensive care unit (PICU). When your child is suffering from acute kidney injury, in the PICU they are monitored by checking the blood levels of serum creatinine and measuring the urine output during a given time, both of these will tell us about the status of kidney function. If any of these parameters i.e. any rise in serum creatinine level or any decrease in urine output of your child is identified they will be still closely monitored, and appropriate measures will be taken to minimize the kidney injury. It will also help to prevent your child from further progressing to chronic kidney disease.

By this study we will also know whether which stage your child condition is and will help us to decide when to intervene, and also help the treating health professional to use particular staging to diagnose Acute Kidney Injury.

Participation in this study is purely voluntary, and that refusal to participate will not involve any penalty or loss of benefits to which you are otherwise entitled. All details including personal data will be kept highly confidential.

In case of doubts/ questions, please contact:

1. Dr. C. Priyalatha,
   Department of Paediatrics,
   Christian Medical College,
   Vellore - 632004
   Mobile no: 9443019661

கிறிஸ்துவ மருத்துவ கல்லூரி, வேலூர்.
குழந்தை மருத்துவயியல் துறை

ஆய்வில் கலந்து கொள்வதற்கான ஒப்புதல் அறிவிப்பு படிவம்

ஆய்வின் தலைப்பு :

குழந்தைகள் தீவிர சிகிச்சை பிரிவில் அனுமதிக்கப்பட்ட குழந்தைகளின் வெவ்வேறு சிறுநீரக செயலிழப்பு குறியீடுகளை கொண்டு தீவிரமான சீறுநீரக பாதிப்பு ஏற்படுவதைப் பற்றிய ஆய்வு

ஆய்வு எண் : .....

பங்குபெறுபவரின் பெயர் : .....

பிறந்த தேதி / வயது :

1) இந்த ஆய்வுக்கான ..... தேதியிட்ட நோயாளியின் தகவல் படிவத்தை படித்து புரிந்துகொண்டேன். கேள்வி கேட்கும் வாய்ப்பினையும் பெற்றேன் என உறுதியளிக்கின்றேன். ( )

2) இந்த ஆய்வில் பங்கு பெறுதல் என் தனிப்பட்ட விருப்பம் என்றும் புரிந்துக் கொண்டேன். மேலும் என் வழக்கமான சிகிச்சையையோ அல்லது என் உரிமைகளோ பாதிக்காமல் எந்நேரத்திலும் என் அனுமதியை விலக்கிக்கொள்ளலாம் எனவும் தெரிந்துக்கொண்டேன். ( )

3) இந்த ஆய்வின் ஆதரவாளருக்காக பணிபுரிபவர்கள் நெறிமுறை குழுவினர் மற்றும் கட்டுப்பாட்டு அதிகாரிகள் என்னுடைய சம்மதம் இன்றி என் உடல்நல பதிவேடுகளை இந்த ஆய்வுக்காகவும் இது தொடர்பான எதிர்கால ஆய்வுகளுக்காகவும், நான் இந்த ஆய்வில் இருந்து விலகிய போதிலும் பயன்படுத்திக்கொள்ளலாம். அதற்கு நான் அனுமதி அளிக்கின்றேன். மேலும் எனது அடையாளம் எவ்வித மூன்றாம் கட்சி மற்றும் வெளியீட்டாளர்களின் தகவல் வெளியீடுகளிலும் வெளியிடப்படாது என்பதையும் நான் அறிந்துக்கொண்டேன். ( )

4) இந்த ஆய்வின் மூலம் பெறப்படும் தரவு மற்றும் முடிவுகளை எவ்வித தடையுமின்றி அறிவியல் நோக்கத்திற்கு மட்டுமே பயன்படுத்தப்படும் என்பதை ஒப்புக்கொண்டேன். ( )

5) மேற்கண்ட ஆய்வில் பங்குபெற நான் தன்னிச்சையாக ஒப்புதல் அளிக்கிறேன். ( )

பெயர் :
பங்கு பெறுபவரின் / சட்டபூர்வமான பிரதிநிதியின் :
கையொப்பம் / கைரேகை :
தேதி

சாட்சியாளரின் பெயர் :
பங்குபெறுபவரின் உறவுமுறை கையொப்பம் :
தேதி

सूचना पत्र

बीमार बच्चो मे तीव्र गुर्दे की विफलता को नापने के लिए सूचकानाको के इस्तेमाल का अध्ययन

गुर्दे की तीव्र विफलता एक सामान्य कारण है जिसके लिए बच्चे आय सी यू मे भरती किए जाते है . आय सी यू मे गुर्दे की हालत देखने के लिए खून मे क्रियतिनीन रसायन और पेशाब के उत्पादन की जाच की जाती है. अगर खून मे क्रियतिनीन बढ़ता है या पेशाब का उत्पादन कम हो जाता है तो गुर्दे की हालत ज़्यादा खराब होती है. अगर ऐसा होता है तो आपके बच्चे का निकट से ध्यान रखा जाएगा और गुर्दे को बचाने की कोशिश होगी. इससे गुर्दे की विफलता को जीर्ण होने से रोका जाएगा.

इस अध्ययन से हमे ये पता चलेगा की बच्चे की स्तिति किस चरण पर है और कब और क्या चिकित्सा की जाए.

इस अध्ययन मे भाग लेना स्वैच्छिक है और भाग ना लेने पर आपके इलाज पर कोई फ़र्क नही पड़ेगा. आपकी निजी जानकारी गोपनिए रखी जाएगी.

किसी भी प्रश्ना या शक के लिए संपर्क करे :

डॉ सी. प्रियलता

बाल चिकित्सा विभाग

क्रिस्चियन मेडिकल कॉलेज

वेल्लोरे - 632004

मोबाइल नो - 9443019661

CONSENT FORM

Format for Informed Consent Form for Parent / Guardian of the Subjects

Informed Consent form to participate in a research study

Study Title:

Study Number: _____

Subject's Initials: _____ Subject's Name: _____

Date of Birth / Age: _____

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my son / daughter's participation in the study is voluntary and that he/she is free to withdraw at any time, without giving any reason, without his/her medical care or legal rights being affected. [ ]

(iii) I understand that the Ethics Committee and the regulatory authorities will not need my permission to look at my son / daughter's health records both in respect of the current study and any further research that may be conducted in relation to it, even if he/she withdraws from the trial. I agree to this access. However, I understand that my son / daughter identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree for the participation of my son/daughter in the above study. [ ]

Signature (or Thumb impression) of the Subject's parent /Legally Acceptable Guardian
Date: _____/_____/_____
Signatory's Name: _____
Signature: _____
Or
Representative: _____
Date: _____/_____/_____
Signatory's Name: _____

Signature or thumb impression of the Witness: _____
Date: _____/_____/_____
Name & Address of the Witness: _____

கிறிஸ்துவ மருத்துவ கல்லூரி, வேலூர்.
குழந்தை மருத்துவயியல் துறை

ஆய்வில் கலந்து கொள்வதற்கான ஒப்புதல் அறிவிப்பு படிவம்

ஆய்வின் தலைப்பு :

குழந்தைகள் தீவிர சிகிச்சை பிரிவில் அனுமதிக்கப்பட்ட குழந்தைகளின் வெவ்வேறு சிறுநீரக செயலிழப்பு குறியீடுகளை கொண்டு தீவிரமான சிறுநீரக பாதிப்பு ஏற்படுவதைப் பற்றிய ஆய்வு

ஆய்வு எண் : .....

பங்குபெறுபவரின் பெயர் : .....

பிறந்த தேதி / வயது :

1) இந்த ஆய்வுக்கான ..... தேதியிட்ட நோயாளியின் தகவல் படிவத்தை படித்து புரிந்துகொண்டேன். கேள்வி கேட்கும் வாய்ப்பினையும் பெற்றேன் என உறுதியளிக்கின்றேன். ( )

2) இந்த ஆய்வில் பங்கு பெறுதல் என் தனிப்பட்ட விருப்பம் என்றும் புரிந்துக் கொண்டேன். மேலும் என் வழக்கமான சிகிச்சையையோ அல்லது என் உரிமைகளோ பாதிக்காமல் எந்நேரத்திலும் என் அனுமதியை விலக்கிக்கொள்ளலாம் எனவும் தெரிந்துக்கொண்டேன். ( )

3) இந்த ஆய்வின் ஆதரவாளருக்காக பணிபுரிபவர்கள் நெறிமுறை குழுவினர் மற்றும் கட்டுப்பாட்டு அதிகாரிகள் என்னுடைய சம்மதம் இன்றி என் உடல்நல பதிவேடுகளை இந்த ஆய்வுக்காகவும் இது தொடர்பான எதிர்கால ஆய்வுகளுக்காகவும், நான் இந்த ஆய்வில் இருந்து விலகிய போதிலும் பயன்படுத்திக்கொள்ளலாம். அதற்கு நான் அனுமதி அளிக்கின்றேன். மேலும் எனது அடையாளம் எவ்வித மூன்றாம் கட்சி மற்றும் வெளியீட்டாளர்களின் தகவல் வெளியீடுகளிலும் வெளியிடப்படாது என்பதையும் நான் அறிந்துக்கொண்டேன். ( )

4) இந்த ஆய்வின் மூலம் பெறப்படும் தரவு மற்றும் முடிவுகளை எவ்வித தடையுமின்றி அறிவியல் நோக்கத்திற்கு மட்டுமே பயன்படுத்தப்படும் என்பதை ஒப்புக்கொண்டேன். ( )

5) மேற்கண்ட ஆய்வில் பங்குபெற நான் தன்னிச்சையாக ஒப்புதல் அளிக்கிறேன். ( )

सूचित सहमति पत्र

आधायन में भाग लेने की सहमति
आधायन का शीर्षक :- - बीमार बच्चो मे तीव्र गुर्दे की विफलता को नापने के लिए सूचकानाको के इस्तेमाल का अध्ययन
अध्ययन क्रमांक :- _____
मरीज़ का नाम :- _____
जन्म तिथि / उमर :- _____

(१) मैं पुष्टि करता हू की मैने _____ तारीख को सूचना पत्र पढ़ा है और सवाल पूछे है.

(२) मैं समझता हू की इस आधायन में मेरी भागीदारी स्वैच्छिक है और मैं किसी भी समय अपनी भागीदारी वापस ले सकता हू, बिना कोई कारण बताए और इससे मेरी चिकित्सा पर कोई फ़र्क नही पड़ेगा .

(३) मैं समझता हू की इस आदयायन के प्रायोजक, प्रायोजक क़ी ओर से काम कर रहे अन्य लोग, आचार समिति और चनयामक अचिकाररयों को मेरे स्वास्थ्या रेकॉर्ड्स देखने के लिए मेरी अनुमचत क़ी जरूरत नहीं होगी. मेरी पहचान तीसरे पक्ष को जारी या प्रकाशित नही की जाएगी .

(४) मैं इस अध्ययन की जानकारी और परिणाम का इस्तेमाल केवल वैज्ञाचनक उद्देश्य (ओं) के लिए प्रदान करता हू

(५) मैं इस अध्ययन में भाग लेने की सहमति देता हू .

IRB APPROVAL

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

October 19, 2016.

Dr. C. Priyalatha,
PG Registrar,
Department of Paediatrics II,
Christian Medical College,
Vellore – 632 002.

Sub: **Fluid Research Grant NEW PROPOSAL:**
Study of Acute Kidney Injury in critically ill children using different renal failure indices.
Dr. C. Priyalatha, (emp. No. 30626), PG Registrar, Paediatric, Dr. Indira Agarwal (Emp. No. 13171), Dr. Kala Ebenezer (Emp. No. 20049), Paediatric Intensive, Dr. Rohit Bhowmick (Emp. No. 81626), Paediatrics II, Dr. Visalakshi Jeyaseelan (Emp. No. 31093), Biostatistics

Ref: IRB Min. No. 10306 dated 12.10.2016

Dear Dr. C. Priyalatha,

The Institutional Review Board (**Blue**, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "Study of Acute Kidney Injury in critically ill children using different renal failure indices." on October 12th 2016. I am quoting below the minutes of the meeting.

The Committee raises the following queries:

1. Will you exclude children who come into ICU with AKI
2. Is a creatinine done everyday on all patients in ICU
3. Will all children be catheterized even if they don't need a catheter
4. Are you going to exclude immunocompromised patients
5. What are the outcomes being studied
6. List of publications needs a full reference including journal, year etc
7. What criteria will be used to define AKI
8. What are the risk factors that you are going to look at – mention all the risk factors in your write up
9. Are you going to look at renal outcome or overall outcome
10. There are duplicate documents in your admission
11. No name , phone number not available in information sheet
12. No need for sample size in the information sheet
13. You need a parent consent form and a child assent form.
14. Need translation into vernacular language.

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in

Dr. B.J. Prashantham, M.A., M.A., Dr. Min (Clinical)
Director, Christian Counseling Center,
Chairperson, Ethics Committee.

Dr. Anna Benjamin Pulimood, M.B.B.S., MD., Ph.D.,
Chairperson, Research Committee & Principal

Dr. Biju George, M.B.B.S., MD., DM.,
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Drs C. Priyalatha and Indira Agarwal was present during the presentation of the proposal and satisfactorily responded to the queries raised by the Members. After discussion, it was resolved to **ACCEPT the proposal after receiving the suggested modifications and answers to the queries.**

Note:
1. Kindly HIGHLIGHT the modifications in the revised proposal.
2. Keep a covering letter and point out the answer to the queries.
3. Reply to the queries should be submitted within 3 months duration from the time of the thesis/ protocol presentation, if not the thesis/protocol have to be resubmitted to the IRB.
4. The checklist has to be sent along with the answers to queries.

Email the details to research@cmcvellore.ac.in and send a hard copy through internal dispatch to Dr. Biju George, Addl. Vice-Principal (Research), Principal's Office, CMC.

Yours sincerely,

Dr. Biju George
Secretary (Ethics Committee)
Institutional Review Board.

CHRISTIAN MEDICAL COLLEGE VELLORE
Dr. BIJU GEORGE
MBBS., MD., DM.,
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board (CMC)
Christian Medical College, Vellore - 632 002.

Cc: Dr. Indira Agarwal, Department of Paediatrics IT, CMC, Vellore.

Ethics Committee Blue, Office of Research, 1st Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788, 2284481 E-mail: research@cmcvellore.ac.in